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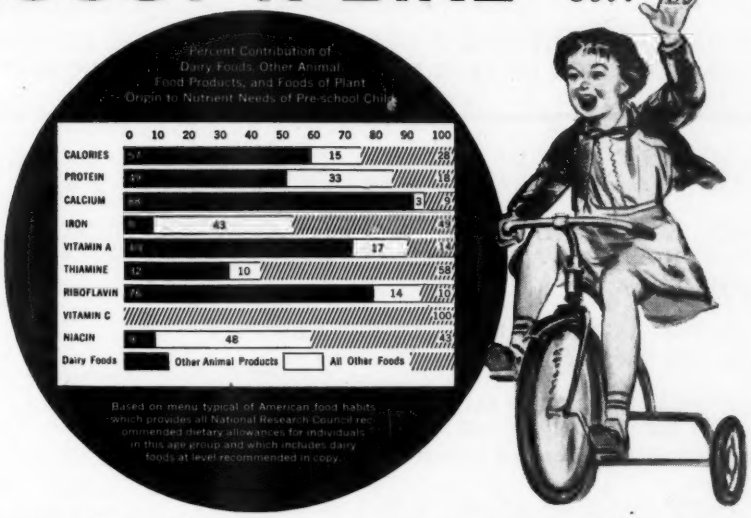
Percent Contribution of Dairy Foods, Other Animal Food Products, and Foods of Plant Origin to Nutrient Needs of Pre-school Child
0 10 20 30 40 50 60 70 80 90 100
CALORIES
PROTEIN
CALCIUM
IRON
VITAMIN A
THIAMINE
RIBOFLAVIN
VITAMIN C
NIACIN
15
33
3
43
17
10
14
48
Dairy Foods
Other Animal Products
All Other Foods
Based on menu typical of American food habits which provides all National Research Council recommended dietary allowances for individuals in this age group and which includes dairy foods at level recommended in copy.

Learning to ride a bike or pushing a doll buggy around the block are part of the pre-schoolers big job of growing up — so is learning to eat a variety of foods, to meet the nutrient needs of growth and to establish good eating habits for a healthy life.

Protein is essential for the child's developing muscle, and for growth of bone as well. Milk and milk products are the primary source of protein in the diet of young children.[1] Eggs, meat, fish and poultry are also sources of high quality protein and should be included in the child's diet.

Calcium, phosphorus, and vitamin D are required for the normal calcification of bones and teeth, a continuous process during growth . . . even during the period of slow linear growth. One quart of vitamin D fortified milk per day will provide adequate quantities of these nutrients during pre-school years.[1]

Iron, copper, and certain other minerals are needed for red blood cell formation and as catalysts in various enzyme systems. These nutrients are provided by eggs, meats, fish, fruits, vegetables, and whole grain or enriched cereals.

All the essential vitamins must be provided for the formation and functioning of normal body tissues. Milk and milk products are the main source of *riboflavin* and of pre-formed *vitamin A* in children's diets . . . and provide some of all the other known vitamins.

Whole grain or enriched cereals and legumes supplement dairy foods and meats as sources of the *B-vitamins*. Citrus fruits, tomatoes, and other fruits and vegetables are needed as a source of vitamin C . . . and provide liberal amounts of vitamin A as well.

Energy for growth and activity is provided by all foods. More than 85 percent of the necessary calories come from fats and carbohydrates,[2] both of which are needed for adequate nutrition of the young child.[1] Butterfat is an excellent and dependable dietary fat for children of this age group.

Approximately one quart of milk, or its equivalent in other dairy foods—cheese, ice cream and butter—is recommended for inclusion in the diet of the normal young child every day.

[1]Jeans, P. C. Feeding of healthy infants and children. J. Am. Med. Assn. *142*:807 (March) 1950.
[2]*The National Food Situation.* NFS—60 U. S. Department of Agriculture, Washington, D.C. (April-June) 1952.

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A Critical Appraisal of THE DIETARY MANAGEMENT *of* PEPTIC ULCER *and* ULCERATIVE COLITIS

By STEWART WOLF, M.D.*

IT IS PRETTY well agreed that the treatment of peptic ulcer, whether it is located in the stomach or duodenum, consists of inhibiting, neutralizing, or diluting the excessive secretion of corrosive gastric juice. The possibilities of neutralizing and diluting are limited because the stomach of the patient with peptic ulcer is an hypermotile one which empties itself rapidly and frequently. Inhibition of gastric secretion with drugs has also been of limited value because the drugs also inhibit other cholinergic functions and can, therefore, be used in only limited quantities. Gastric secretion in duodenal ulcer may be increased as much as tenfold. To most physicians, the medical therapy of peptic ulcer is largely a matter of diet. What can be expected of manipulating the diet, in terms of inhibition of gastric function or of promoting healing of an ulcer? The most physiologic way of inhibiting gastric function is by the ingestion of a fat-containing meal. The natural subsidence of the brisk increase in gastric function which accompanies eating appears to depend upon the effects of fat absorption toward the end of the period of gastric digestion. Observations of this effect were made on the fistulous subject, Tom, and reported in detail elsewhere.[1]

In Figure 1 are shown diagrammatically the results of ingestion of a normal fat-containing breakfast (on the left) in comparison with a fat-free breakfast (on the right). Five and one-half hours after a normal fat-containing breakfast there was still a little breakfast present in the stomach, but acidity was low and motor activity modest and intermittent. This normal tapering-off process failed to occur when fat was omitted from the meal. In the middle graph are shown the effects of a fat-containing breakfast, eaten in a setting of anxiety and tension. The usual inhibitory effects of fat were entirely outweighed by the stimulating effects of the situation. Only five hours after a meal the stomach was completely empty of recognizable breakfast. Titratable acid was 100 units and motor activity was unusually vigorous. This experiment, which illustrates the comparative effects of two opposing forces acting on the stomach, explains why one cannot count very heavily on the inhibitory effects of diet in peptic ulcer, especially when the stomach is under stimulation from meaningful events in the individual's daily life.

Neither is there much evidence that the wrong food can accelerate gastric function,

From the Department of Medicine, University of Oklahoma School of Medicine and the Oklahoma Medical Research Foundation, Oklahoma City, Okla.

* Professor of Medicine and Chairman of the Department, University of Oklahoma School of Medicine.

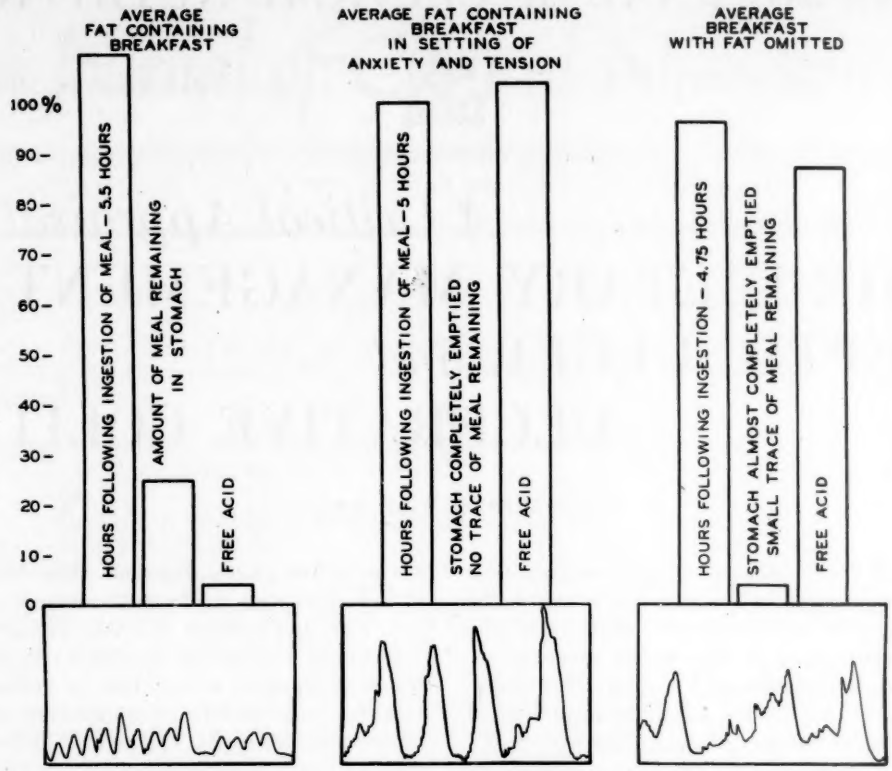

Fig. 1. Gastric function approximately 5 hours following the ingestion of a meal. Sample tracings of motor activity in the gastric antrum are shown in the blocks below the columns.

although coffee and alcohol promote increased gastric acidity and, therefore, might profitably be eliminated from the diet. Most foods other than fats and notably protein, are capable of accelerating gastric function. Among these are essential elements in the diet which cannot be eliminated. The stimulating effects of food, however, are transitory and not very vigorous in comparison to the stimulating effects of life situations.

Some dietary prescriptions are based on the notion that certain articles of diet are irritating to the stomach. Accordingly, various foods were placed directly into the stomach of our fistulous subject, Tom. Observations were made at times when the stomach was hyperemic and overactive from the standpoint of acid secretion and motor activity, as well as when it was in its pale, inactive state. The gastric mucosa was carefully scrutinized, not only with the naked eye but also with a dissecting microscope, so that subtle changes could be detected. No foods, including chile con carne, were found to be irritating to the stomach. At a later date these observations were repeated on a fistulous subject who had an active duodenal ulcer. Again, there was no evidence of irritation or other recognizable effects. Finally, chemicals and other substances such as strong condiments were applied directly to the stomachs of Tom and of the patient with peptic ulcer. Each substance was also applied simultaneously to the skin of the forearm. As shown in Table I, it was found that the skin of the forearm was far more vulnerable to irritants than was the lining of the stomach.

It would appear that the treatment of peptic ulcer is the treatment of gastric hyperfunction and that measures which do not have a

TABLE I

Comparison of the Effects of Various Substances on the Gastric Mucosa and the Skin of the Forearm

	Gastric mucosa	Forearm
Alcohol 50%	0	++
Alcohol 100%	0	++
Digitalis	0	0
Ferrous sulfate	0	0
Mustard (1–30 susp. in water)	++	++++++
1 *N* HCl	++	++++++
0.1 *N* NaOH	++	++++++

\+ = slight erythema. ++++++ = vesiculation and destruction of tissue.
++++ = wheal formation.
Other pluses indicate intermediate grades of change.

significant bearing on gastric function have little relevance in the treatment of peptic ulcer. As far as diet is concerned, it is evidently important to provide feedings that are frequent enough so that the stomach will not remain empty, and it is also important that these feedings contain milk and cream, which do as well at neutralizing and inhibiting gastric function as can be done. The addition of nonabsorbable alkalies and antispasmodics is probably worth while but of limited value. The most pertinent steps in the management of patients with peptic ulcer are concerned with a consideration of the person in the patient, including attempts to help him deal more constructively with problems and challenges in his day-to-day life. Certainly, before prescribing limitations to the diets of persons with peptic ulcer, we need better evidence that ordinary foods are either stimulating or irritating to the stomach.

Ulcerative Colitis

The treatment of ulcerative colitis is also bound up with dietary rituals for which we have relatively little concrete evidence. It appears that the fundamental disturbance in ulcerative colitis is one of colonic hyperfunction with hyperemia, engorgement, and intense hypermotility of the gut. This has been shown to be associated with the great increase in fragility of the membrane, with easy ulceration. Ulcerations have been produced in a segment of gut which was disconnected from the fecal stream and not subject to any local irritation by seeds, skins, or vegetable fibers. The ulcerations occurred in a setting of intense emotional conflict. Certain foods, such as prunes, have cathartic properties and it seems logical to eliminate these from the diet of a patient with ulcerative colitis.

The presence of bulk in the colon is a natural stimulus to peristaltic activity, but by no means an essential one. A completely empty colon has been shown to engage in most intense and persistent contractile activity following stimuli arising out of the life situation.

In ulcerative colitis, the gastrocolic reflex has been shown to be greatly exaggerated, even when the colon has been disconnected from the rest of the alimentary tract. Thus, the effect does not depend upon any food actually coming into contact with the mucous membrane of the colon. It therefore appears that the ingredients of the feces with respect to residual food constituents have very little to do with colonic hyperfunction or ulceration. A series of 35 patients with ulcerative colitis of varying severity treated by Grace completely without reference to diet, but with major consideration of the life adjustment, did considerably better in a three-year follow-up than a group of carefully matched cases who were treated by traditional means including dietary restriction.[2] The comparative figures are shown in Table II.

TABLE II

Ulcerative Colitis

Results of treatment of ulcerative colitis in a special clinic compared to the results achieved in a comparable group as closely matched as possible and treated in other clinics of the hospital.

Totals	Died	Operations	Worse	Same	Improved	Symptom free
Med. A (34)	3 = 9%	1 = 3%	0	8 = 23%	13 = 39%	9 = 26%
Match (34)	6 = 18%	10* = 29%	2 = 6%	7 = 21%	6 = 18%	5 = 15%

* Two died following operation.

Undue regimentation or restriction may lead either to malnutrition or to frustration and resentment on the part of the patient, with deleterious effects which far outweigh the beneficial effects of the diet. On the other hand, a carefully balanced diet which involves a certain amount of ritual may have a very salutary psychological effect on an overmeticulous, compulsive patient. In such a case, however, one must not carelessly attribute favorable results to the intrinsic merits of the foods.

Summary

Evidence is presented which suggests that settings of anxiety and tension can nullify the beneficial effects of a high fat meal on gastric acidity and motility. One should not count very heavily on the inhibitory effects of diet in peptic ulcer when the stomach is under stimulation from stressful situations in the patient's daily life. There is also a great need to study the true effects of certain so-called irritating foods, condiments, and chemicals on the stomach. In a fistulous subject, the direct application of commonly accepted irritants produced fewer and lesser changes in the stomach than on the skin.

Similarly, the colon in ulcerative colitis responds more violently to certain situational stimuli than to foods and fecal contents.

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Resumen

Apreciación crítica del tratamiento dietético de la úlcera péptica y de la colitis ulcerosa

Se presenta evidencia que sugiere que períodos de ansiedad y tensión pueden nulificar los efectos benéficos de una comida rica en grasas sobre la motilidad y acidéz gástrica. No se puede confiar completamente en los efectos inhibitorios de la dieta en la úlcera péptica cuando el estómago se encuentra bajo la influencia de situaciones tensionales que ocurren en la vida diaria del paciente. Existe también la necesidad de un estudio completo de los verdaderos efectos que producen en el estómago los llamados alimentos irritantes, condimentos y substancias químicas. En un individuo fistuloso la aplicación directa de los irritantes comunmente aceptados producen cambios menores en el estómago que en la piel.

De un modo similar, el colon en la colitis ulcerosa responde más violentamente a ciertos estímulos emocionales que a los alimentos y al contenido fecal.

NUTRITIONAL ASPECTS of HEART FAILURE

By CHARLES R. SHUMAN, M.D.,* AND MICHAEL G. WOHL, M.D.†

THE CARDIAC patient, like the normal person, should be maintained in nutritional homeostasis. His diet should be patterned as closely as possible after his "normal" diet, provided three objectives are achieved: reducing the work of the heart, preventing or eliminating edema, and establishing nutritional balance for calories, protein, and essential food factors. In addition, the food plan offered must be acceptable to the patient in order to insure its successful enforcement.

The problem of maintaining the nutritional status of patients with congestive heart failure is complicated by several factors. One of the least understood, yet probably most important, is the alteration in cellular metabolism resulting from chronic congestive circulatory failure. This is manifested by electrolyte shifts and a change in water balance within the body.[1-4] A reduction of cellular protein and potassium and an increase in intracellular sodium and water have been demonstrated. Alterations in the osmotic relationships between intra- and extracellular fluid compartments have been postulated on the basis of these metabolic adjustments.[2] Another important contributing factor is the loss of body protein observed in cardiac decompensation. Not only is this phenomenon manifested by the frequent finding of hyproteinemia and hypoalbuminemia,[5-9] but also it is apparent in the muscle atrophy and wasting, especially pronounced in the upper extremities and pectoral regions, of the chronically decompensated patient. Since the cellular electrolyte structure is not altered in compensated cardiac patients, it is probable that the shifts observed in heart failure are, in part, related to the disturbance in protein metabolism.

The total body protein deficits calculated from the value of total circulating albumin indicate an extensive reduction in congestive failure. Assuming a normal blood volume as shown by Ross *et al.*,[10] the total circulating albumin can be estimated. According to Elman,[11] each gram of circulating protein below normal is equivalent to a loss of 30 Gm. of tissue protein. With movement of water into the cells, the values for tissue protein may actually be somewhat lower than these estimates. The loss of muscle mass seen on examination may be a gross reflection of this protein deficiency. Actual measurements of the nitrogen content of skeletal muscle in congestive failure patients at biopsy disclosed reductions of protein below control values.[1]

The loss of cellular protein, and the associated electrolyte and fluid shifts, may prevent the effective utilization of co-enzyme by the cells in the formation of active enzyme.

EFFECT OF CIRCULATORY FAILURE ON NUTRITION

In heart failure, there are basic difficulties in the absorption and utilization of foodstuffs. The reduced appetite limits the actual intake of food, particularly meat and other protein sources. The assimilation of digested foods is impaired by the reduced transport rates in the absorption pathways of the gastrointestinal and portal systems. The dynamic activity of the gastrointestinal mucosal cells may be af-

From Nutrition Project, Philadelphia General Hospital and Temple University School of Medicine.

* Associate in Medicine, Temple University School of Medicine and Hospital, Philadelphia.

† Clinical Professor of Medicine, Temple University School of Medicine and Hospital, Chief of the Nutrition Clinic, Philadelphia General Hospital, Senior Attending Physician, Albert Einstein Medical Center, Philadelphia.

fected by an alteration in electrolyte concentrations and by anoxia. Furthermore, the rate of utilization of the absorbed nutrients by the liver is impaired due to the alterations in liver function—a common finding in heart failure.[12] In each of these crucial phases, it is the protein and vitamin metabolism which are especially susceptible to the damaging effects of cardiac failure. Thus, using radioactive iodine and sulphate labeled amino acids, the rate of protein turnover in congestive failure has been shown to be strikingly prolonged by Armstrong and co-workers.[13]

Therapeutic Agents

In addition to the nutritional impairment wrought by anoxia and the circulatory defects of cardiac failure, certain problems arise in connection with the agents employed in its treatment. The use of digitalis and ammonium chloride may produce anorexia and nausea which further reduce the dietary intake. Sodium restriction and the administration of mercurial diuretics under certain circumstances may lead to disturbances in electrolyte balance which further impair cellular function.

Thiamine Metabolism

We have recently studied the effect of mercurial diuretics upon thiamine excretion in nine patients with chronic cardiac decompensation.[14] These subjects manifested signs of progressive heart failure despite treatment with digitalis, diuretics, salt-poor diets, and vitamin supplementation. The excretion of thiamine was measured in 24-hour urine samples obtained after vitamins and mercurial diuretics were withheld for three days. During the control period the mean 24-hour thiamine output was 134.9 μg. The mean 24-hour thiamine excretions on the day of the mercurial injection and the day following the mercurial were 403.2 μg. and 419.4 μg., respectively. These observations suggest that one effect of mercurial diuretics is to increase both the concentration and absolute amounts of thiamine in the urine. Our data also indicate that the mercurial-induced thiamine loss is not a function of the increased urine volume. The most likely explanation is depression of renal tubular reabsorption of thiamine.[15]

In order to study the status of thiamine nutrition in patients with heart disease, 35 subjects admitted to the Philadelphia General Hospital for the treatment of congestive failure were examined by means of a thiamine loading test using an intramuscular injection of 0.35 mg. of thiamine per square meter of surface area.[16] The thiamine excretion over a four-hour period after the loading dose was measured by the method of Melnick and Field.[17] Similar studies were performed in a group of 17 normal controls. The mean thiamine excretion for the 35 cardiac patients was 40.6 μg.; the mean thiamine excretion for controls was 139.5 μg. These findings demonstrate a significant difference between the two groups. The failure of the cardiac patients to excrete thiamine in amounts comparable to normal subjects is interpreted as retention of the vitamin within the tissues to restore the depleted cocarboxylase (diphosphothiamine) levels. Our results are in agreement with those of Robinson and Melnick[18] and others who have found evidence of thiamine deficiency in patients with cardiac decompensation.

Preliminary studies on the thiamine and cocarboxylase content of tissues of 9 patients who died in cardiac failure and 7 control patients who died from noncardiac causes showed statistically significant lower concentration of both total thiamine and cocarboxylase in the heart tissue of patients with heart failure than in the control patients. In liver tissue the difference between the groups was significant for total thiamine but not for cocarboxylase. In kidney tissue the differences were not statistically significant.[19] The determination of blood cocarboxylase in cases of heart failure by Goodhart and Sinclair[20] revealed subnormal values in 6 of 13 patients examined. Thus, ample evidence has accumulated to suggest the presence of subclinical thiamine deficiency in at least some patients with severe congestive failure. The mechanisms operating to produce this condition may include inadequate dietary intake, interference with absorption and utilization of thiamine for cocarboxylase formation, and the increased excretion of thiamine

resulting from the use of mercurial diuretics.

The depletion of tissue cocarboxylase may prevent the utilization of carbohydrate-derived substrate for energy production. However, large decreases of thiamine are required before pyruvate utilization is impaired.[21] This results in a rise in blood lactate and pyruvate which has been demonstrated to exist in congestive failure.[22,23] Furthermore, other nutrients may be used by the myocardium for purposes of energy formation.[24] However, if the energy derived from noncarbohydrate sources were sufficient to maintain the requirements of the myocardium, the existence of beriberi heart disease would be difficult to explain. It is well known that patients with this disease respond poorly to digitalis but recover upon administration of thiamine.

A possible effect of these changes upon the myocardium may be that of further reducing efficiency and rendering the maintenance of compensation more difficult. Furthermore, with a rise of blood pyruvate and lactate there is an associated vasodilation with a resultant rise in cardiac output.[25] There is experimental evidence that deficiency of thiamine, as well as of other fractions of the vitamin B complex (biotin and pantothenic acid), results in lessened ability of heart slices to utilize acetate and pyruvate.[26] The work of Bing[27] using coronary sinus catheterization suggests that there is no defect in oxidative metabolism in heart failure but that the primary difficulty lies in the conversion of the energy derived from these sources into mechanical work. Although this may be true in the early stages of decompensated heart disease, it is possible that in the more resistant later phases of heart failure the biochemical defect of a low capacity for energy formation is also involved.

Relation to Potassium

It is interesting to note that the electrocardiographic changes observed in thiamine deficiency resemble those described in hypopotassemia; namely, a prolonged QT interval with low, broad T waves.[28] Experimental thiamine depletion in animals was found by Pecora to be associated with abnormally low concentrations of potassium in the myocardium.[29] These animals also manifested an increased intracellular sodium content and evidence of water retention.[29] Similar findings in the biochemical analysis of tissues obtained from congestive failure patients suggest that the low thiamine content observed in this condition may be related, in some way, to electrolyte alteration.

Dietary Problems

The recognition of protein and vitamin deficiencies in chronic congestive failure has prompted the administration of large quantities of dietary protein and supplemental vitamins to patients with this disorder. Some difficulties are encountered in augmenting the protein component of the diet because of the necessity for restricting the salt intake. Several dialyzed salt-free milk preparations, flavored with various agents, have been employed, and natural protein foods, such as meats, eggs, and cheese have been fed together with sodium-exchanging resins. The intravenous administration of amino acids and salt-free albumin has been cautiously attempted in a few instances. Vitamin supplementation has been used orally and parenterally in most of the patients examined in the thiamine excretion studies. It has been recommended that 100 mg. of thiamine daily be given to patients with congestive failure. Our present investigations indicate that there is no advantage in the administration of thiamine in quantities larger than 10 mg. daily, parenterally, in correcting the subclinical deficiencies detected by the loading test method.

The patients found to be in congestive failure resistant to the usual therapeutic measures have not always been benefited by efforts at protein and vitamin replacement. However, long-term observations on patients seen in early phases of heart failure with special attention to the maintenance of the nutritional status has not been made. The problem of overcoming anorexia, absorption and utilization defects, and alterations in cellular metabolism are formidable obstacles confronting the physician concerned with the nutritional aspects of cardiac disease.

Clinical Aspects

The indices which denote the precarious nutritional status of many patients with chronic congestive failure are (1) hypoproteinemia, which may act synergistically with salt and water retention and increased venous pressure to produce edema, (2) evidence of muscle wasting reflecting the losses of tissue protein, and (3) the presence of subclinical vitamin deficiencies, especially of thiamine. Our studies have demonstrated and reaffirmed the findings of a deficiency of thiamine nutrition in cardiac patients and have revealed a high incidence of hypoproteinemia and muscle wasting. In addition, we have shown that the use of mercurial diuretics has increased the urinary excretion rate of thiamine.

Diet Patterns—Therapeutic Salt Restricted Diet

The basic foods required in the diet to provide adequate nutrients must receive primary consideration:

> Milk—1 pint; meat—4 ounces; vegetables—2 servings; fruit and fruit juices—3 servings; carbohydrate and fat to fulfill caloric needs.

In order to restore depleted protein levels, it is necessary to increase the protein component by adding meat servings. The caloric requirement of the diet is based upon the body weight of the patient with respect to the desired weight. One may encounter hypoproteinemia in overweight persons. In these instances, we have encouraged high level protein feedings (1.5 to 2.0 Gm. per Kg. body weight) with restriction of carbohydrate. There is evidence to indicate that protein repletion can occur despite caloric restriction under these circumstances, the energy requirements being satisfied by endogenous fat sources.[30,31]

Having fulfilled the dietary requirements for protein, accessory food factors, and calories, the problem of the sodium restriction must be resolved. By employing the following measures the sodium intake can be restricted to an average of 0.6 Gm.:

> Avoid canned foods unless prepared without salt. Use unsalted breads and fats. Avoid frozen peas and lima beans; avoid fresh beets and celery. Use no preserved foods, meats, fruits, flour mixes, or relishes containing salt. Avoid instant coffees and Dutch processed cocoa. Shellfish, except oysters, should be excluded.

For more strenuous salt restriction to the level of 200–400 mg. per day, the use of a low sodium milk such as Lanolac® or Lesofac® is necessary. For high-level protein feedings with sharp sodium restriction various low sodium meat and milk products must be employed. Several salt substitutes such as Co-Salt,® Neocurtasal,® and Diasal® may be recommended for flavoring. These contain ammonium and potassium chloride and may be used in the absence of serious renal insufficiency. Lemon juice, dry mustard, and pepper may also be employed for the seasoning of food. If the basic foods are included in the diet, vitamin supplementation may not be required. However, if diuretics are necessary in the management of fluid retention, the administration of a balanced vitamin preparation orally, or preferably parenterally, is recommended.

Attention to these details should provide an adequate diet to accomplish the objectives of the dietary management of heart disease. However, our ability to influence the defects of absorption and utilization of ingested foodstuffs has not improved. Further study of these aspects of the problem is indicated.

Summary

The nutritional status of patients with congestive heart failure becomes increasingly important as cardiac decompensation advances. While it is true that early in the course of decompensated heart disease no nutritional defects may be encountered, in the resistant phases of chronic heart failure serious nutritional alterations occur. These include changes in electrolytes and water balance, hypoproteinemia, and subclinical thiamine deficiency. Factors contributing to thiamine deficiency

are anorexia and impaired absorption and utilization of nutrients. The conventional use of mercurial diuretics may constitute an additional factor by increasing thiamine excretion, although it is realized that mercurial diuretics are of basic importance in cardiac therapy. Suggestions are made for supplying a dietary program including an adequate protein intake, restricted in salt, supplemented by oral or parenteral vitamin therapy.

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RESUMEN

Aspectos nutricionales de la insuficiencia cardíaca

El estado nutricional de los pacientes con insuficiencia cardíaca congestiva se vuelve más importante cuando la descompensación progresa. Mientras al principio de la descompensación pueden no encontrarse defectos nutricionales, en las fases resistentes de la insuficiencia cardíaca ocurren serias alteraciones en la nutrición. Estas incluyen cambios en los balances del agua y de los electrolitos, hipoproteinemia y deficiencia subclínica de tiamina. Los factores que contribuyen para la producción de la deficiencia de tiamina son la anorexia y la defectuosa absorción y utilización de las substancias nutritivas. El uso convencional de los diuréticos mercuriales puede constituir un factor adicional incrementando la excreción de tiamina, aunque as reconocido la importancia básica que los diuréticos mercuriales tienen en la terapía cardíaca. Se sugiere un programa dietetico que incluye una cantidad adecuada de proteínas, restricción de sal y adición de vitaminas administradas por vía oral y parenteral.

Current Status of VITAMIN THERAPY *in* NERVOUS *and* MENTAL DISEASE

By ROBERT A. PETERMAN, M.D.* AND ROBERT S. GOODHART, M.D.†

As a result of the greatly expanded activity in the various research fields directly or indirectly related to medicine and metabolism, much light has been shed on hitherto relatively unknown or unexplored areas of cellular metabolism. New concepts of diseases and their treatment have been formed or are now forming, and certain previously indistinct avenues of research have been clearly defined.

Realization of the importance of understanding individual tissue cell metabolism and the relation of this to the body as a whole grows continually. Daily the normal human body must absorb about four or five ounces of glucose, slightly more than one ounce of a proper mixture of amino acids, two or three ounces of fat or oil, milligram quantities of vitamins and minerals, and one or two quarts of water. With these specific chemical substances the body grows, builds, repairs, defends, and reproduces itself, and performs all its functions and actions. The signs and symptoms of many diseases and disorders are the results of interference at one or more points along the metabolic pathways of these materials. Destruction or impaired function of relatively few cells in a metabolically important tissue or structure can lead, directly or indirectly, to undesirable effects upon the total organism. Health, at any level and in any tissue, is directly dependent upon maintenance of structure and proper function of the individual cells.

From the Washington Heights Nutrition Clinic, Bureau of Nutrition, New York City Department of Health, and The National Vitamin Foundation, Incorporated.

* Formerly Clinic Physician, Washington Heights Nutrition Clinic.

† Scientific Director, The National Vitamin Foundation, Inc., New York.

The Nervous System

Essentially, the nervous system is a communication system and its chief function is dependent upon the proper production, release, regeneration, storage, and transmission of energy. In comparison with other mechanisms, the information on metabolic energy production is relatively abundant[1] and the chief sources of energy for the nervous system have been fairly well established.[1,2]

The chief source of energy for the nervous system is glucose,[2] which is progressively fragmented within the cell and ultimately reduced stepwise to carbon dioxide and water. Numerous chemical pathways for energy release in the catabolic destruction of glucose exist, but the currently available evidence indicates that in the nervous system this is accomplished by a combination of two well-known series of reactions, namely Embden-Meyerhof glycolysis and the citric acid (Krebs) cycle.[1-4] In both series of cleavage and oxidation reactions energy release occurs at several points(Fig. 1). The process consists essentially of the releasing of hydrogen, each hydrogen atom producing one electron of energy. At each step, a specific enzyme system is involved wherein, essentially, a hydrogen group is plucked from the orbit of a carbon atom of the carbohydrate fragment. As the hydrogen atom chemically satisfies the waiting receptor of the enzyme, the energy becomes available by virtue of an increased potential (hydrogen ion concentration) of the system. In so doing, the enzyme

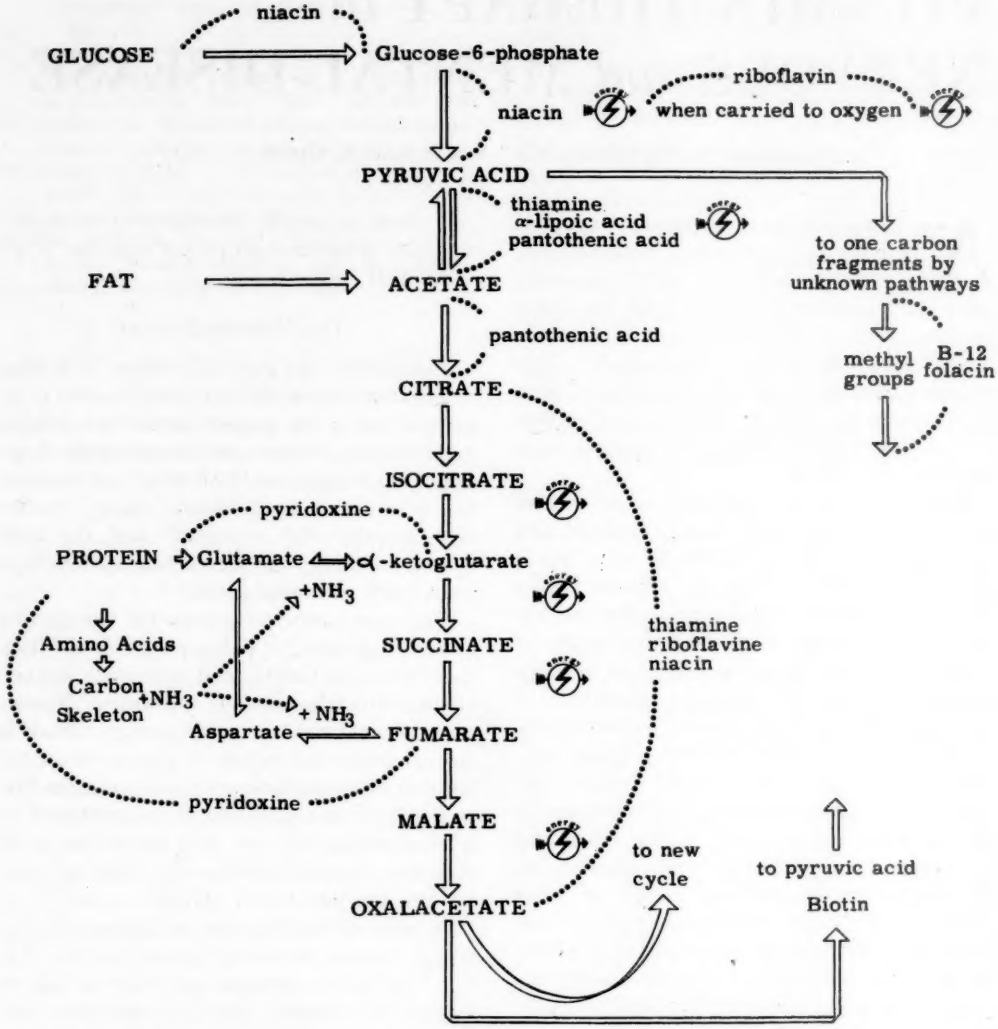

Fig. 1. Principal sources of energy for the nervous system (adapted from Sebrell[1] and Umbreit[5,7]).

system itself is converted or neutralized by means of another separate "side" cycle. The principal enzyme substance is promptly "recharged" and made ready for the next glucose fragment which comes its way.[2,3,5] Fat can contribute energy through the carbohydrate moiety which enters the cycle as a metabolic fragment at the acetate level. Energy also can be obtained from protein sources; however, the only clearly established protein source of energy for the brain is derived from glutamic acid which is converted to alpha-ketogluturate and enters the citric acid (Krebs) cycle at this level.[1] Ammonia (NH_3) groups obtained from deamination of other amino acids may contribute indirectly at the aspartate-fumarate stage of the cycle.[6]

The nutritional significance of all this is that fragmentation of molecules, the energy release mechanisms, the enzyme regeneration cycles, and the disposal mechanisms are all directly or indirectly dependent upon the various *vitamins* which act in the role of enzymes, parts of enzymes, co-enzymes, or catalysts.

The importance of energy production to the function of the nervous system, plus the importance of the roles played by the vitamins, provide an explanation for the occurrence of such symptoms as mental confusion or irritability, inability to concentrate, paresthesias, dysesthesias, inco-ordination, ataxia, and others which have been directly correlated with various vitamin deficiency states but for which pathologic tissue changes have not been demonstrated.[1,8]

Certain of the multiple but ill-defined pains and unpleasant sensations complained of by the neurasthenic may be due to a failure of proper energy production or regeneration, as a result of low-grade, long-term (single or multiple) vitamin deficiency. The often reported prompt relief of such ill-defined complaints following the administration of B-complex vitamin preparations to neurasthenics may well represent more than suggestive therapy on occasion.

The maintenance of structure and the prompt and maximal repair of tissue following injury are obviously essential in maintaining or restoring normal function. That certain vitamins, particularly those of the B-complex, are essential in the maintenance of structure and function of the nervous system has been well established by laboratory and animal studies and by direct clinical correlation.[7,8,10,14,15,16]

Although the knowledge of the biochemical mechanisms and metabolic pathways involved in tissue synthesis, replacement, and repair is small and incomplete, a number of fundamental points have been well established.[1] The essential roles of a number of the vitamins have also been demonstrated in the synthesis of new cells and the formation of metabolic materials, such as antibodies, blood albumin and globulins, certain hormones, hemoglobin, and similar substances containing protein.

Furthermore, the formation and action of some nonprotein metabolic substances such as acetylcholine are dependent upon the presence of certain vitamins. For example, in the performance of muscular work the following is recognized: an electrical (nerve) impulse activates the end plate of a motor nerve in a muscle. This action, possibly by reconverting an electron of energy to a hydrogen or some other atom by changes in potential, initiates a series of chemical steps which result in the freeing of an inactive stored form of acetylcholine at the end plate. This in turn activates another chain of chemical reactions which utilizes locally stored fuel (glycogen) and converts it into the energy needed for muscular contraction. Following the contraction, the waste products must be neutralized or carried away, the energy release mechanism recharged, and the local fuel store replaced. In addition, the acetylcholine formed, having performed its function, must be inactivated and the motor end plate itself must be "recharged" in readiness for the next conversion of electrical to physical energy.[5,9] Each of these small but necessary steps is dependent upon the presence of one or more of the vitamins acting either directly or indirectly in the enzyme system (Table I).

At this point, the physician reader may justifiably ask: "How can this information be applied, in practical action, in the treatment of the patient or the prevention of disease?";

TABLE I

Metabolic Roles of Various Vitamins Directly or Indirectly Related to Nervous System Metabolism

Thiamine (1,2,5,7,8,9,11,12–16,21,22)*	—Essential for energy release and regeneration mechanisms. —Acts as a catalyst in disposal of pyruvic acid and lactic acid and as a co-ferment with acetylcholine in the humoral stimulation of the nervous system. —Participates in intermediary carbohydrate metabolism and decarboxylation of α-keto-acids. —Intensifies the action of acetylcholine. —In the transformation of pyruvate to acetate may act as the compound lipothiamid diphosphate.
Riboflavin (1,5,7,8,10,14,15,16)	—Indispensable in energy metabolism and important in tissue synthesis. —An essential constituent of the yellow enzyme (flavoprotein) which is present in all living cells. It functions as an oxygen carrier between molecular oxygen and substrate in association with other oxidative systems.
Niacin (Niacinamide) (1,7,8,10,14,15,16)	—Important in both energy metabolism and tissue synthesis. —A component of two important co-enzymes: co-enzyme I (cozymase) and co-enzyme II (co-ferment). These are essential in glycolysis and tissue respiration. —Acts as a hydrogen carrier in dehydrogenation reactions of carbohydrate metabolism. —Necessary for the function of specific protein enzymes. —Necessary in acetylcholine synthesis. —Has been identified with more than 40 oxidation-reduction reactions involved in energy release and tissue synthesis.
Pantothenic Acid (1,7,8,10,14,15,16,19,20,21,27)	—Forms active portion of the co-enzyme A molecule which is essential for acetylation reactions. —Necessary in detoxification of organic substances, inorganic poisons, and certain therapeutic agents such as the sulfonamide drugs. —Essential in carbohydrate oxidation in formation of citric acid from oxalacetic acid. —Involved in the formation of acetylcholine, steroids, fatty acids, amino acids, and phospholipids. —Acts as acetate mediator in many specific enzymatic reactions; reactive acetyl compounds from pyruvate and other sources transfer acetate to a variety of acceptors.
Pyridoxine (1,7,8,10,14–19)	—Converted to the co-enzyme, pyridoxal phosphate, required by at least 15 known enzyme systems. —Essential for intracellular protein formation and utilization, maintenance, repair and growth of tissue, antibody formation, and hormone formation and function. —Necessary for energy release in work performance, production of nerve impulse, and provision of chemical energy to activate anabolic (building) reactions. —Instrumental in the transformation of glutamic acid to α-ketoglutaric acid in the citric acid cycle.[1] —Participates in detoxification or neutralization reactions. —Deamination of amino acids to α-keto-acids catalyzed by pyridoxal phosphate—connects amino acid metabolism to carbohydrate formation and utilization.[1] —Necessary for proper functioning of other B-complex vitamins.
Cyanocobalamin (Vitamin B_{12}) (6,7,8,10,14,15,16,23–34,76)	—Acts as a catalyst and possibly a co-enzyme in cellular transmethylation reactions. —Essential in nucleic acid metabolism which regulates cell function, probably involved in both ribose and desoxyribose metabolism. —Probably related to sulfhydryl (SH) mechanisms in detoxification and tissue synthesis. —Believed to exert a significant influence on energy metabolism.
Folacin (7,8,10,14,32,33,34)	—Essential in desoxyribose nucleic acid metabolism.
Biotin (1,7,8,10,15,35,36,37)	—Apparently essential in carboxylase reactions leading to aspartic acid. Also active in many CO_2 fixation reactions.
Ascorbic Acid (7–10,15,38,39,40)	—Essential for maintenance of normal intercellular material of connective tissue. —Important in activation of acetylcholine and consequently in the transmission of the nerve impulse.
Vitamin A (7,8,15,41,42)	—Essential in retinene-rhodopsin (visual purple) cycle in retina of eye.

* Figures in parentheses refer to reference numbers at end of article.

Vitamin D (7,8,15,43,44)	—May indirectly be involved in carbohydrate metabolism through its effect on phosphate metabolism.
Choline (1,7,8,10,14,15,45, 46)	—Not identified with specific enzyme activity but is a dietary source of essential labile methyl groups and is an integrating part of the lecithin molecule and of acetylcholine. May, therefore, be important as a building stone for constituents of nervous tissue.
Inositol (1,7,8,10,14,15,45, 46)	—Not identified with specific enzyme activity, but appears to be a building stone for lipositols and for phosphotides.

"What are the symptoms and signs which will alert the practicing physician to the existence of some unrecognized or otherwise undetectable disorder?"; and "What can be done about it therapeutically?"

In answer, it should be pointed out first that vitamin or nutritional deficiencies have been established as etiologic factors in a number of specific neurological disorders (Table II).

Clinical and Morphological Findings

In Table III, symptoms and findings associated with certain vitamin deficiencies are listed. Emphasis has been placed upon early symptoms, where such have been established, since early recognition of disorders provides an opportunity to prevent further regression or the development of undesirable complica-

TABLE II

Examples of Specific Disorders or Symptom Complexes Involving the Nervous System Wherein a Vitamin Deficiency has been Found to Play an Etiologic Role or Which May be Prevented or Relieved in Part or Completely by the Administration of Certain Vitamins (1, 8, 10, 14, 15, 16, 18, 34, 47–57)*

Disorder	Vitamin Involved
Wernicke's Syndrome	Thiamine and B-Complex
Toxic (Alcohol and Tobacco) Amblyopia	Thiamine and B-Complex
Combined System Disease	Vitamin B_{12}
Niacin Deficiency Encephalopathy (Alcoholic or Nutritional Encephalopathy)	Niacin
Ménière's Syndrome	Niacin, Riboflavin and B-Complex
Mental Deterioration or Depression	Niacin and B-Complex
Metabolic Neuritis (Nutritional Polyneuropathy)—Occurs in Alcoholism, Pellagra, Beriberi, Gastrointestinal Dysfunction, Hysteria, Psychoses, Diabetes, Pregnancy, Pernicious Anemia, and Other Chronic Diseases	Thiamine, Vitamin B_{12}, Vitamin B_6, Folic Acid, and B-Complex
Trigeminal Neuritis	Vitamin B_{12} and B-Complex
Epileptiform Convulsions of Vitamin B_6 Deficiency in Infants	Vitamin B_6
Nutritional Melalgia (Burning Foot Syndrome)	Pantothenic Acid
Myasthenia Gravis	Pantothenic Acid

* Figures in parentheses refer to reference numbers at end of article.

TABLE III

Symptoms and Findings Related to the Nervous System Described in Certain Vitamin Deficiency States

Vitamin	Clinical reports	Experimental and laboratory findings
Thiamine (1,8,10,14,15,16,53–59, 62)*	Anorexia, constipation, forgetfulness, difficulty in orderly thinking, ideas of persecution, headache, insomnia, vertigo, burning sensations, cramping, and tenderness of muscles. Other findings include: ascending symmetrical peripheral neuritis with pain and weakness, hyperthesia—early, anesthesia—late, loss of vibration sense, Achilles and patellar reflex changes, increased early, then diminished, finally absent—also retrobulbar neuritis, scotomata and oculomotor palsies.	Diminution of glucose and oxygen utilization (human). Congestion and edema of brain and spinal cord. Chromatolysis, swollen and dislocated nuclei in posterior spinal ganglion, anterior horn cells and ganglion cells of medulla and pons. Degeneration of medullary sheaths in all tracts of the cord especially the posterior columns. Degenerative changes in peripheral nerves, cranial nerves (especially the vagi), cardiac plexus, splanchnic nerves, solar and renal plexus—characterized by fragmentation and atrophy of axis cylinders and degeneration of myelin sheath.

* Figures in parentheses refer to reference numbers at end of article.

TABLE III (continued)

Vitamin	Clinical reports	Experimental and laboratory findings
Riboflavin (8,10,14,15,16)	Headache, dizziness, mental depression, insomnia, visual disturbances, forgetfulness, mild states of mental confusion, inability to concentrate and perform mental work, photophobia, burning sensations in skin, anorexia, weakness and keratitis and vascularization of the cornea.	Nerve degeneration in rats, ataxia, spasticity, and muscular weakness in dogs, inco-ordination in monkeys, inco-ordination and nerve degeneration in swine, and "curled-toe" paralysis in chicks. Also keratitis and corneal vascularization in rats.
Niacin (Niacinamide) (1,8,10,14,15,16,52, 53, 58)	Depression, apprehension, increased irritability, insomnia, headaches, dizziness, muscular weakness and symptom complexes characteristic of neurasthenia, anxiety states or other neuroses. Later: Memory loss, excitement, mania, delirium, hallucinations, dementia, tremor; jerky movements frequently accompany the mental symptoms.	Myelin degeneration and axonal reaction affecting both the central and peripheral nerves (in dogs with black tongue).
Pantothenic Acid (1,8,10,14,15,16,48, 60,61)	Administration of calcium pantothenate reported to have relieved nutritional melalgia (burning foot syndrome) in soldiers, and to be of benefit in certain cases of myasthenia gravis; reported to have relieved paralytic ileus. Administration of large doses, prior to cold stress, prevents certain metabolic changes which may have an indirect effect upon the nervous system.	Degenerative spinal cord lesions in chicks. Convulsions in dogs. In rats, transitory maternal deficiency produces abnormalities in brain and eyes of offspring. In swine, severe neurologic involvement characterized by a spastic ataxic gait and degenerative lesions in both sensory and motor component.
Pyridoxine (1,8,10,14–18,47)	Convulsions (epileptiform), weakness, insomnia, irritability, and difficulty in walking, peripheral neuritis indistinguishable from that of thiamine deficiency neuritis. Vitamin B_6 therapy reported to reduce number and severity of seizures in certain patients with epilepsy. Vitamin B_6 therapy reported to produce additional improvement in pellagrins (including neurologic disorders) after maximal effect from niacin, riboflavin, and thiamine.	Epileptiform seizures in the chick, rat, dog, and pig. Demyelinization of peripheral nerves in the dog. Interference with glutamic acid metabolism in the brain (*in vitro*).
Cyanocobalamin (Vitamin B_{12}) (8,10,15,16,24,31,49, 50,51,63,66,76)	Combined system disease of pernicious anemia. (All phases—mental, central, and peripheral.) Vitamin B_{12} therapy reported to benefit diabetic neuritis: pain, paresthesia, plantar dysesthesia, reflex changes, atony of bladder; tic douloureux and trigeminal neuritis (certain cases); lightning pains of tabes dorsalis; postherpetic neuralgia; toxic neuritides (certain cases); peripheral neuritis, radiculitis, causalgia and phantom limb pain (certain cases).	Characteristic changes observed in neurologic structures of vitamin B_{12} deficient rats include: Reduction in ribose nucleic acid. Increased lipid in myelinated fibers with loss of definition and globulization of lipid. Increased sudanophilia near nucleus and streaming from nuclear to cell membrane. Increased neuronolysis. In humans: Histochemical changes in sympathetic ganglion similar in some respects to those observed in vitamin B_{12}—deficient rats reverted toward normal following administration of vitamin B_{12} (change characterized by increase in nucleic acid, reduction of neuronolysis, and improvement in definition of structure).
Biotin (1,15,35)	Mental symptoms characterized by a confused, depressed mental state with hallucinations and anorexia (experimental —the work has not been repeated).	In rats, biotin deficiency causes spasticity of hind quarters, arching of back, and progressive paralysis.

Vitamin	Clinical reports	Experimental and laboratory findings
Ascorbic Acid (8,9,15)	Hypersensitivity to touch and mental derangement have been reported in scurvy; convulsions and paralysis have been described. Vitamin C therapy has been reported to have been instrumental in preventing or relieving the neuritis of lead poisoning.	Peripheral nerve degeneration and changes in the motor cells in the anterior horns (guinea pig).
Vitamin A (8,15)	Night blindness.	In animals, degeneration of the medulla oblongata and of the cochlear neurons has occurred with resulting deafness.

tions. The symptoms listed may occur in a variety of diseases and metabolic disorders; however, the possibility that, when occurring in disorders or diseases other than primary nutritional deficiency states, they may be the result of conditioned or local vitamin deficiencies should not be overlooked, and in such instances, therapeutic trial of a vitamin or group of vitamins often is indicated.

Although the classical physical signs of vitamin deficiencies are well known, it would be remiss not to list them briefly here. Their presence in a patient should alert the physician to the necessity of a more careful examination, plus the devotion of special attention to the patient's nutritional status and history (Table IV).

TABLE IV

Physical Findings and Signs Associated with Vitamin and Nutritional Deficiencies and Imbalance[15]

(NOTE: These signs are not always pathognomonic of vitamin deficiencies, but are suggestive and may represent actual deficiency.)

Site	Finding
Hair	Dry, staring, alopecia.
Scalp	Seborrheic dermatitis.
Eyes	Thickened conjunctiva, vascularization of cornea, Bitot's spots, blepharitis.
Lips and mouth angles	Rhagades, cheilosis, increased fissuring, perleche.
Buccal mucosa membranes	Inflammation.
Tongue	Edema, fissuring, prominence or atrophy of papillae, color changes.
Gums	Blunted papillae, inflammation, edema, recession, atrophy.
Skin	Dryness, crinkling (senile-like), follicular hyperkeratosis, dyssebacea, ichthyosis.
Neurologic	Plantar dysesthesia, diminution in vibratory sense, diminished to absent tendon reflexes.

TIME FACTOR

At this point it is important to emphasize that in evaluating the physical signs of vitamin deficiency, the time factor must be considered. It is well established that the rate at which a deficiency develops influences the type of symptoms produced.[64,65] On the other hand, the severity of the deficiency lesion itself frequently bears little relationship to the relative degree of depletion of the body. Therefore, from the clinical standpoint, the discovery of a lesion suggestive of a vitamin deficiency does not establish its existence, but makes mandatory further evaluation of the patient's nutritional status. On the other hand, such a finding coupled with a positive history of nutritional imbalance plus, in certain cases, confirmatory evidence from laboratory studies, does complete the diagnosis and warrants indicated vitamin and nutritional therapy. Clinical laboratory aids to diagnosis in therapeutic nutrition are available and increasingly useful. It is beyond the scope of this report to classify them and discuss their interpretation. The reader is referred to standard texts on the subject.[8,15,19,66]

CONDITIONING FACTORS

The nutritional history is important. Where a qualified nutritionist is available, such an individual should be assigned the responsibility of obtaining the nutritional and dietary history. However, such a detailed and precise evaluation is impossible in many circumstances. Recognition of the existence of a nutritional imbalance or condition which may adversely affect the patient can be achieved by a brief history which takes into account the factors listed in Table V. The existence of one of these situations, combined with symp-

TABLE V

Factors Other Than Primary Food Deficiency Which Produce Undernutrition or Decrease Vitamin Reserves[15,16]

Diminished Food Intake	
Loss of appetite	Trauma, pain, oral disorders
Therapeutic or fad diets	Pregnancy
Food allergy	Mental disorders
Acute or chronic disease	Certain therapeutic agents
Gastrointestinal disorders	Anaesthesia, sedation
Interference with Intestinal Absorption or Destruction of Vitamins in Intestinal Tract	
Absence of digestive enzymes	Decreased absorption area
Unfavorable intestinal flora	Impaired absorption mechanisms
Hypermotility	Certain therapeutic or toxic agents
Increased Metabolic Requirements	
Excessive caloric intake	Pregnancy and lactation
Increased physical activity	Endocrine imbalance
Infection	Trauma, hemorrhage, wound healing
Fever	Toxic agents
Rapid Growth	Certain therapeutic agents
Impairment in Utilization or Storage	
Liver disease	Vitamin deficiency itself
Endocrine imbalance	
Increased Loss or Excretion	
Serous exudates, blood loss	Lactation
Albuminuria, glycosuria	Diuresis

toms and signs that suggest a vitamin imbalance, justifies the administration of the indicated vitamin or nutritional therapy.

Principles of Therapy

Vitamin and nutritional therapy can be divided into three types; specific therapy, general or supportive therapy, and prevention.

The general principles of nutritional therapy consist of providing the necessary nutrient intake by the oral route, supplemented or replaced when necessary by parenteral feeding. When it is impossible or undesirable to provide for adequate nutritional balance by diet alone, supplemental administration of individual or multiple vitamin preparations is indicated—the combination and dosage to be tailored to the needs of the individual patient as determined by the nutritional evaluation.

By *specific therapy* is meant the administration of individual nutrients or combinations of selected nutrients based on the characteristics of the patient's disorder. The indications for thiamine, niacin, riboflavin, and vitamin B_{12} in the treatment of certain neurologic disorders are clear and well known. On the other hand, the indications for pyridoxine and pantothenic acid, both important and metabolically essential vitamins, are not defined. Biotin is unquestionably involved in energy release mechanisms but its need also has not yet been defined. The same holds true for folic acid, which unquestionably is a metabolically essential vitamin and seemingly must be involved, indirectly at least, in energy formation cycles.

Therapeutic levels of the vitamins range generally about 5 to 10 times higher than recommended maintenance levels. With vitamin therapy, unlike certain drug therapy, the response may not be immediate and therapeutic dosage levels may have to be repeated daily for a considerable period of time. On the other hand, with few exceptions, there is little justification for the administration of tremendous and unreasonably high doses, although there is little likelihood of danger from this; it is known that renal thresholds do exist for most of the B-complex vitamins and as a result most of a massive dose is promptly "wasted" in the urine. In true deficiency, tissue uptake is relatively slow and depends upon a chemically balanced mechanism, i.e., the vitamins cannot be "forced-in" with one dose. Instead, as mentioned above, regular daily administration of ordinarily recommended therapeutic dosage levels will be the most desirable.[68]

Several exceptions to this have been reported. For example, it appears that a greater response in a larger number of patients with diabetic neuritis can be obtained by the daily administration of what now appear to be very large doses of vitamin B_{12}.[51] This phenomenon has not been explained but may represent a mass-action effect or the momentary overwhelming of a biochemical threshold as a

result of the temporary high blood levels achieved.

Finally, *prevention* represents another large area which offers, perhaps, the greatest promise. The research literature is relatively replete with examples of increased damage from various stress conditions such as pregnancy[69-72] or from drugs, chemicals, and, on occasion, bacterial toxins when certain vitamin deficiencies are present.[8,10,15] In each such instance, the damage or effect can be minimized or prevented by the administration of the vitamin or essential nutrients prior to or at the time of exposure to the potentially damaging agent.[73] Antibody formation in animals has been shown to be influenced by the presence or absence of certain vitamins, such as pantothenic acid, pyridoxine, and folic acid[74] and it is reasonable to assume that this eventually will be shown to apply for the human as well.

Summary

The status of vitamin therapy in neurologic disorders has been reviewed, and the importance and roles of the vitamins in biochemical or metabolic mechanisms have been shown. Vitamin deficiency signs and symptoms and their correlation with neurologic disorders are discussed and some recommendations on therapy made.

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RESUMEN

Estado actual de la vitaminoterapía en las enfermedades mentales y nerviosas

Se hace un análisis del estado actual de la vitaminoterapía en desórdenes neurológicos y se demuestra la importancia y el papel de las vitaminas en los procesos bioquímicos o metabólicos. Se discuten los signos y síntomas de las deficiencias vitamínicas en correlación con desórdenes neurológicos y se hacen algunas recomendaciones terapéuticas. Son bien conocidas las indicaciones de la tiamina, niacina, riboflavina y vitamina B_{12} para el tratamiento de ciertos desórdenes neurológicos. Por otra parte, aunque la piridoxina y el ácido pantoténico son vitaminas importantes y esenciales para el metabolismo, sus indicaciones no son definidas. Sin lugar a duda la biotina juega un papel importante en el mecanismo de liberación de energía, pero su necesidad no ha sido precisada todavía. Lo mismo sucede con respecto al ácido fólico, el cual indudablemente es una vitamina esencial para el metabolismo y debe jugar un papel, por lo mismo indirecto, en la formación de ciclos de energía.

Los niveles vitamínicos terapéuticos son generalmente entre 5 y 10 veces más altos que los recomendados para mantenimiento. A desemejanza de lo que ocurre con las drogas, en vitaminoterapía la respuesta puede no ser inmediata, pudiendo necesitarse la repetición diaria de las dosis terapéuticas por un considerable período de tiempo. Por otra parte, con pocas excepciones, existe muy poca justificación para el uso de dosis extremadamente altas. En las verdaderas deficiencias la asimilación por parte de los tejidos es relativamente lenta y depende de un mecanismo químico bien balanceado; por lo tanto las vitaminas no pueden ser forzadas en una sola dosis, siendo mas deseable la administración diaria y regular de dosis terapéuticas. Sin embargo, existen excepciones. Por ejemplo, parece que en un gran número de pacientes con neuritis diabética se puede obtener una mejor respuesta con la administración diaria de vitamina B_{12} en dosis que por ahora parecen ser muy grandes.

La prevención constituye otro de los campos importantes. El incremento de los daños producidos como consecuencia de variadas situaciones tensionales que ocurren cuando existen ciertas deficiencias vitamínicas pueden ser reducidas al mínimo o prevenidas con la administración de vitaminas o substancias nutritivas esenciales antes o durante la exposición a los agentes dañinos potenciales.

NUTRITIONAL *Studies of* JUVENILE DIABETICS *Attending Summer Camp*

By HARRY G. JACOBI, M.D.*

With the technical assistance of Mildred Kaufman, B.S., M.S., and Tami Ogata, A.B., M.S.

IT IS INDEED very seldom that one has the opportunity to observe as large a group of diabetic children, under normal healthy environmental conditions and activities, as one sees during their period of stay at a summer camp organized for such children.

In a previous paper[1] the complete routine and organization of the camp project known as Camp NYDA, which is operated by the New York Diabetes Association, was given. The fundamentals underlying such organization were discussed and the established procedures described in detail.

It is now our purpose to report some of our observations and findings with respect to certain nutritional studies that were made on these juvenile diabetics during their camp stay.

CLINICAL MATERIAL

There were a total of 166 diabetic children who attended the summer session of 1951 at Camp NYDA. Eleven of these represented repeat campers who stayed for more than one session, so that actually only 155 individual cases were handled. Of these, 74 were boys and 81 girls. These ranged in age from 6 to 17 years for the boys and 5 to 16 years for the girls. The greatest number of boys were found in the 13- and 14-year-old groups, while a majority of the girls were in the 11- and 15-year-old groups (Table I).

TABLE I

Duration of Diabetes in the Children Forming the Basis of This Report

Duration, Years	Boys	Girls	Total
0–1	16	16	32
1½–2	15	15	30
2½–3	10	12	22
4–5	16	13	29
6–10	15	21	36
11–15	2	4	6
TOTAL	74	81	155

NUTRITIONAL STATUS

In Table II is shown the analysis of the male campers, whose weights and heights are individually compared to normal standards for each respective age, and also the relationship of such weights to each individual height. These comparisons were made from tables of mean weight, mean height, and average weight for height prepared by Bird T. Baldwin, Ph.D., and Thomas D. Wood, M.D., for the American Child Health Association. Children were classified as "mean" when their height was within a half inch of the mean stated, and when their weight at the end of their camp stay was within a pound of the weight stated in the tables. According to these standards 37.8% of our male group were below normal height for age and 40.6% were above normal. Thus there were slightly more who were overheight than underheight. As regards the weight for all, there were 50% who were underweight, 6.8% who were normal weight, and 43.2% who were overweight. When each boy,

111 East 80th Street, New York 21, N. Y.

*Chairman, Camp Committee N.Y.D.A., Summer 1951.

TABLE II

Male—Comparison of Diabetic Children with Normal in Relation to Weight-Height and Weight for Height*

Age	Number	Height			Weight			Relation, weight to height		
		Under	Average	Above	Under	Average	Above	Under	Average	Above
17	2	2	—	—	2	—	—	1	1	—
16	3	—	1	2	1	—	2	2	—	1
15	5	3	1	1	4	—	1	2	1	2
14	12	4	3	5	6	—	6	6	2	4
13	12	3	1	8	5	—	7	5	4	3
12	7	3	2	2	2	1	4	1	2	4
11	6	2	2	2	2	3	1	2	2	2
10	10	4	3	3	8	—	2	4	3	3
9	7	3	1	3	3	—	4	2	3	2
8	5	2	1	2	2	—	3	1	—	4
7	4	2	1	1	2	1	1	2	1	1
6	1	—	—	1	—	—	1	—	1	—
5	—	—	—	—	—	—	—	—	—	—
TOTAL	74	28	16	30	37	5	32	28	20	26
%		37.8	21.6	40.6	50	6.8	43.2	37.8	27	35.2

* Weight-Height-Age Table for Boys of School Age, prepared by Bird T. Baldwin, Ph.D., and Thomas D. Wood, M.D., and published by the American Child Health Association.

TABLE III

Female—Comparison of Diabetic Children with Normal in Relation to Weight-Height and Weight for Height*

Age	Number	Height			Weight			Relation, weight to height		
		Under	Average	Above	Under	Average	Above	Under	Average	Above
17	—									
16	4	3	1	—	1	—	3	1	—	3
15	12	9	—	3	6	—	6	2	—	10
14	9	2	3	4	3	—	6	3	—	6
13	8	3	1	4	4	—	4	6	—	2
12	7	2	2	3	2	—	5	2	1	4
11	12	3	3	6	3	1	8	1	2	9
10	9	3	3	3	—	—	9	1	1	7
9	7	1	4	2	3	1	3	2	2	3
8	4	—	3	1	—	—	4	—	1	3
7	4	—	2	2	1	—	3	1	—	3
6	4	2	—	2	1	1	2	1	1	2
5	1	—	1	—	—	—	1	—	—	1
TOTAL	81	28	23	30	24	3	54	20	8	53
%		34.6	28.4	37.0	29.6	3.7	66.7	24.7	9.9	65.4

* Weight-Height-Age Table for Girls of School Age, prepared by Bird T. Baldwin, Ph.D., and Thomas D. Wood, M.D., and published by the American Child Health Association.

however, was compared as an individual in reference to his weight-to-height relationship, there still were more who were underweight than were overweight. These figures for weight-to-height relationship showed 37.8% underweight and 35.2% above normal weight, with 27% normal. Thus this latter relationship comparison increased the number of normals for the boys from 6.8 to 27%.

In similar studies with data from the girls, the picture is quite different. Table III reveals that a comparison of diabetic and normal girls in relation to height for age reveals 34.6% were underheight, 28.4% of average height, and 37% overheight. With respect to their weight for age relationship, 29.6% were underweight, 3.7% were normal, and 66.7% were overweight. When, however, weight for

individual height comparisons were made with similar standard relationships there were still 65.4% or about two-thirds of the girls who were overweight, 24.7% who were underweight, and 9.9% who fell into the average range. In particular, the 9- to 12-year-old group fell most frequently into the average category.

Dietary Intake

Table IV contains the figures calculated for the boys of each age group with regard to their average caloric consumption per kilogram of body weight while attending camp. These were then compared with the recommendations by the Food and Nutrition Board of the National Research Council of the United States as determined for normal boys and based upon their ideal body weight. On the whole, there is a good deal of agreement in these figures, with very few exceptions such as the 12-year-old and the 8-year-old who were receiving somewhat fewer calories per Kg. of body weight, while the 13- to 17- and the 6- and 7-year-old were receiving slightly more than the recommended amounts. However, when these figures are compared with those recommended by Barach[2] for diabetics, it may be observed that the caloric consumption of our boys was greater than these averages. On the other hand, comparison of our figures for calories allowed per Kg. of body weight with those based on the average weight for height tables prepared by Baldwin and Wood[3] reveal that ours were slightly less for all except the 7-year-old group.

In Table V the same comparisons are recorded for the girls. Here the calories allowed were slightly less for the 14- to 16-year-olds and also the 5- to 12-year-olds than those given for the ideal body weight and based on figures furnished by the Food and Nutrition Board. Only the 13-year-old girls received more calories per Kg. than those given for their ideal weights. This practice was justified in view of the previously mentioned data shown in Table III indicating a preponderance of overweight among all the girls except in the

TABLE IV

Male—Comparison of Average Calories per Kilogram Allowed for Each Age Group at Camp with Those for Ideal Body Weight and Also Those Recommended for Normal Requirements

Age	Number	Calories/ Kg. body weight	Calories/ Kg. ideal body weight*	Calories/ Kg. recommended by Barach†	Calories/ Kg. recommended‡
17	2	52.9	51.3	43.3	57
16	3	45.1	42.7	44	57
15	5	53.1	51.8	48	60
14	12	52.0	49.7	49	66
13	12	58.5	56.4	55	70
12	7	58.9	62.7	57	72
11	6	69.0	69.1	59	74
10	10	76.2	69.5	63	76
9	7	75.3	76.5	64.5	77
8	5	73.1	77.1	68	77
7	4	103.8	101.5	73	80
6	1	85.0	82.3	79	90

* Food and Nutrition Board, National Research Cuoncil of the United States of America, 1948.

† Nutritional Standards and Treatment of Diabetes Joseph H. Barach, M.D., Falk Clinic, University of Pittsburgh, 1944.

‡ Based on Average Weight for Height Tables, prepared by Bird T. Baldwin, Ph.D., and Thomas D. Wood, M.D.

TABLE V

Female—Comparison of Average Calories per Kilogram Allowed for Each Age Group at Camp with Those for Ideal Body Weight and Also Those Recommended for Normal Requirements

Age	Number	Calories/ Kg. body weight	Calories/ Kg. ideal body weight*	Calories/ Kg. recommended by Barach†	Calories/ Kg. recommended‡
16	4	39.8	43.2	44	49
15	12	45.3	46.9	48	50
14	9	41.9	43.7	49	53
13	8	54.9	52.4	55	58
12	7	48.3	53.2	57	66
11	12	59.0	63.0	59	70.0
10	9	61.7	68.7	63	76
9	7	71.8	72.1	64.5	77
8	4	71.2	74.6	68	77
7	4	74.2	78.7	73	80
6	4	85.6	85.2	79	80
5	1	93.8	97.8	82	84

* Food and Nutrition Board, National Research Council of the United States of America, 1948.

† Nutritional Standards and Treatment of Diabetes, Joseph H. Barach, M.D., Falk Clinic, University of Pittsburgh, 1944.

‡ Based on Average Weight for Height Tables, prepared by Bird T. Baldwin, Ph.D., and Thomas D. Wood, M.D.

TABLE VI

Males—Changes in Diets During Camp Stay

Age	No.	Beginning					End					Diet changes		
		1*	2	3	4	5	1*	2	3	4	5	Dec.	Same	Inc.
17	2	—	—	1	1	—	—	—	1	1	—	—	2	—
16	3	—	2	—	1	—	—	—	—	2	1	—	—	3
15	5	—	—	1	4	—	—	—	1	4	—	—	5	—
14	12	—	2	6	4	—	—	2	3	5	2	—	7	5
13	12	1	6	4	1	—	—	—	7	5	—	—	4	8
12	7	—	4	—	1	2	—	3	1	1	2	1	5	1
11	6	—	2	2	2	—	—	1	3	2	—	1	3	2
10	10	—	7	1	2	—	—	3	4	3	—	—	6	4
9	7	1	3	3	—	—	—	2	4	1	—	—	3	4
8	5	3	1	1	—	—	2	2	1	—	—	—	4	1
7	4	2	2	—	—	—	—	1	3	—	—	—	—	4
6	1	—	1	—	—	—	—	1	—	—	—	—	1	—
5	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	74	7	30	19	16	2	2	15	28	24	5	2	40	32

Camp Diets

Diet	Carbohydrate	Protein	Fat	Total calories
1*	160	95	90	1800
2	200	100	100	2100
3	250	110	110	2400
4	300	120	110	2670
5	325	120	120	2860

13-year-old group where the incidence of overweight to underweight was reversed.

Changes in diets during their camp stay in the case of the boys are shown in Table VI. Here are recorded the number in each age group placed on the various diets both at the beginning of the camp period, and the diets they were on at the end of that period. It will be noted that slightly less than half the boys at the beginning of their camp stay were on Diet 2 (2100 calories). At the end of that period only half of these actually remained on Diet 2, and only two out of seven were allowed to remain on Diet 1; most of those on Diet 2 had to be shifted to Diets 3 and 4 which were higher in caloric value. On the whole, there were 32 boys whose diets had to be increased, and only 2 whose diets were decreased. (This fits in well with our statistical data in Table IV showing that initially our boys were receiving slightly less calories per Kg. of body weight than those based on the figures by Baldwin and Wood.)

A similar comparison for the girls, shown in Table VII reveals quite a different situation. At the beginning of their camp stay 22 were on Diet 1, 35 on Diet 2, 23 on Diet 3, 1 on Diet 4, and none on Diet 5. At the end of the period 4 had their diets reduced, while 57 remained on the same diet as initially indicated, and only 20 required an increase.

Weight Changes

An evaluation was attempted with respect to the actual changes in weight that occurred in the boys' group during their stay at Camp NYDA. Several important points must be taken into consideration in attempting such evaluation. The most important is the experience of *non*diabetic boys with respect to their weight after spending a summer at camp. Most of them lose weight in spite of the large consumption of food, a large proportion of which is in the form of carbohydrates. There is the same factor at work in the case of the diabetic child, except that his carbohydrate intake cannot be increased too generously.

A total of 29 boys, approximately 40%, showed a gain of weight at the end of their stay (Table VIII). Of these, 13 were under-

TABLE VII

Female—Changes in Diet During Camp Stay

Age	No.	Beginning					End					Diet changes		
		1*	2	3	4	5	1*	2	3	4	5	Dec.	Same	Inc.
17	—													
16	4	—	—	3	1	—	—	2	2	—	—	2	2	—
15	12	2	4	6	—	—	2	3	5	1	1	—	9	3
14	9	4	3	2	—	—	3	4	1	1	—	—	7	2
13	8	1	3	4	—	—	1	2	2	3	—	—	4	4
12	7	1	4	2	—	—	1	4	2	—	—	—	7	—
11	12	—	8	4	—	—	—	6	5	1	—	1	8	3
10	9	1	6	2	—	—	1	3	5	—	—	1	4	4
9	7	3	4	—	—	—	2	3	1	1	—	—	5	2
8	4	3	1	—	—	—	2	1	1	—	—	—	2	2
7	4	2	2	—	—	—	2	2	—	—	—	—	4	—
6	4	4	—	—	—	—	4	—	—	—	—	—	4	—
5	—	1	—	—	—	—	1	—	—	—	—	—	1	—
	81	22	35	23	1	—	19	30	24	7	1	4	57	20

Camp Diets

Diet	Carbohydrate	Protein	Fat	Total calories
1*	160	95	90	1800
2	200	100	100	2100
3	250	110	110	2400
4	300	120	110	2670
5	325	120	120	2860

weight, 9 belonged to the group with average weight, and 7 in the overweight group. There were 34 boys, or 46% of the group, who lost weight. Of these, 15, or almost half, belonged to the overweight, 16 to the underweight, and 3 to the average weight group. There were 10 boys, or 14%, whose weight did not change while at camp. Of these, 3 were overweight, 3 were underweight, and 4 were of average weight. There was one boy who was not included here because he was unable to report for his final weighing on account of illness.

TABLE VIII

Analysis of Weight Changes During Camp Stay

Weight change	No.	%	Weight at start of period		
			Under	Average	Over
Boys—74:					
Gain	29	40	13	9	7
Loss	34	46	16	3	15
No change	10	14	3	4	3
Not included in study	1	Unable to report for final weighing due to illness			
Girls—81:					
Gain	28	37	7	2	19
Loss	35	45	7	4	24
No change	15	18	4	2	9
Not included in study	3	Unable to report for final weighing due to illness			

An analysis of the weights of the girls is also shown in Table VIII. There were 28 girls, or approximately 37%, who gained weight while at camp. Most of these were already overweight. There were 35 (45%) who lost weight. Here again, most of these belonged to the overweight group. Finally, there were 15 girls (18%) whose weight remained unchanged. Of these, 9 were overweight, 4 belonged to the underweight, and 2 were in the average weight group.

Types of Insulin and Dosage

An analysis of the various insulins used by the children both at home and while attending camp is shown in Table IX. This reveals that prior to coming to camp half of the boy campers were taking one dose of NPH insulin each day. About a third were taking mixtures of one sort or another. Of these mixtures,

TABLE IX

Analysis of Insulins Used by Children Both at Home and While Attending Camp

Type insulin	Boys				Girls			
	Home		Camp		Home		Camp	
	No.	%	No.	%	No.	%	No.	%
NPH	37	50	38	51	41	50	45	55
Mixtures	23	31	13	17.5	25	30.9	23	28.5
PZI	7	9	16	21.6	7	8.7	7	8.7
Globin	1	1.4	1	1.4	1	1.3	1	1.3
Regular	2	2.9	1	1.4	2	2.6	1	1.3
Mixture plus regular	1	1.4	—	—	1	1.3	—	—
PZI and regular, separate	2	2.9	2	2.9	3	3.9	2	2.6
NPH and regular, separate	—	—	1	1.4	—	—	1	1.3
NPH and PZI, separate	—	—	1	1.4	—	—	—	—
PZI and globin, separate	—	—	—	—	1	1.3	1	1.3
No insulin	1	1.4	1	1.4	—	—	—	—

three were a combination of regular and NPH insulin, while all the rest contained regular and protamine zinc in various proportions, the two-to-one and one-to-one mixtures being the most popular. One boy had been on a combination of a mixture at breakfast time and a dose of regular insulin with the evening meal. There was one male camper in the group who required no insulin while at home and continued to do well while at camp without insulin in spite of the fact that his diet was increased during his camp stay from 1800 to 2400 calories. We of course did not attempt to make any further studies on this case on account of the limitations placed upon us.

By the end of the camp stay one more boy was taking one dose of NPH each day. Those taking mixtures, however, were reduced from 23, or 31%, to 13, or 17.5%. Those on protamine zinc insulin had increased from 7 to 16. Of the two who were on regular insulin alone, only one remained on this preparation.

All home insulin doses were reduced by 30% in determining the dose to be allowed the camper at the beginning of his camp stay. No attempt was made to make any other changes either in the selection of the type of insulin or the time of administration. It is of interest to note (Table X) that during the course of their camp stay 13, or 17.5%, of the boys had to have a further reduction in their insulin dosage beyond the 30% initial reduction from their home insulin dose. In 6 of these, the diet was also increased at the same time, while the remaining 7 were maintained on the same diet. Only 3 boys (4.2%) could be maintained on

TABLE X

Changes in Total Insulin Dosage and Diet While at Camp

Change in total insulin while at camp	Boys					Girls				
			Diet changes					Diet changes		
	No.	%	Dec.	Same	Inc.	No.	%	Dec.	Same	Inc.
Further reduction	13	17.5	—	7	6	11	13.5	—	5	6
Maintained on admission dose	3	4.2	—	3	—	10	12.0	3	7	—
Increased dose but less than home dose	21	28	1	12	8	26	32.5	—	23	3
Increased to home insulin dose	9	12.4	1	5	3	4	5	—	3	1
Increased above home total dose	27	36.5	—	13	14	30	37	1	19	10
No insulin	1	1.4	—	—	1	—	—	—	—	—

the calculated 30% reduced insulin dosage allowed them upon arrival at camp. Their diets also remained the same. Twenty-one of the group (28%) required an increase in insulin dosage above that initially allowed to them upon arrival at camp, but not equal to the amount they had been taking at home. Of this number, 12 were receiving the same diet, 8 required an increase in their diet, and one received a decreased diet. In 9 boys (12.4%) the insulin dosage had to be increased to the amount they had been taking at home. About one-third of the group required an increase in their total insulin dosage which was greater than what they were taking at home. Of this number, 13 were receiving the same diet, and 14 required an increase in their diet during their camp stay.

An analysis of similar data for the female campers is also presented in Table IX. This reveals that prior to coming to camp half of the girl campers were receiving one dose of NPH insulin a day. There was a remarkable similarity in the distribution of insulin regimens between the boys and the girls.

At the end of their camp stay, the number of girl campers receiving NPH had increased from 41 to 45; those on mixtures had decreased from 25 to 23. Of the two on regular insulin, only one remained on this type at the completion of the camp period.

As was the procedure with the male campers, all home insulin doses were reduced by 30% in determining the dose to be allowed at the beginning of the camp stay. Likewise, no attempt was made to change from one insulin to another. Table X shows that 11 of the female campers required a further reduction in their insulin dosage beyond the 30% initial reduction previously mentioned, this in spite of the fact that only 5 of them remained on the same diet, while 6 had their diets increased. Ten girl campers were able to continue on their admission dose while their diet remained the same in only 7, and the other 3 were able to get along on a decrease in their total caloric intake. Twenty-six required an increased dose of insulin above their admission dose, but not as much as they were taking while at home. Only 4 required an increase in their insulin dose back to the amount they were taking while at home. Of these, 3 remained on the same diet, while one had her diet increased. There were 30 girls who required an increase in their total insulin above what they were receiving prior to coming to camp. Of these, only 10 required an increase in their diet, 19 remained on the same diet, and one had her diet decreased.

Discussion

There seems to be some difference of opinion regarding the growth of the juvenile diabetic as compared to the nondiabetic. Joslin, Root, and White,[4] in reporting on a group of pre-insulin era survivors, mentioned that while some of them showed retardation in growth, the average height of the entire series still exceeded the Baldwin and Wood standard average for their age. They suggested at the time that the potential diabetic child was tall. White,[5] 14 years later, reporting a series of 94 cases of juvenile diabetes, concluded that fatigue of the pituitary is the most logical explanation for the underlying mechanism of growth retardation when that is present. Fischer *et al.*[6] felt that diabetic children are tall for their age at the onset of the disease and that the rate of growth thereafter is slower than the average for nondiabetic children. On the other hand, Boyd[7] reported that diabetic children were not above average height at the onset of the disease and that they failed to show any constant trend in height at any time either before or after onset of the disease.

Our figures show that among the boys and girls more were above average height than below. Of the two groups, the boys showed the larger number in the taller group. Brown and Thompson,[8] however, in a study of 60 diabetic children and adolescents who developed diabetes before the age of 15 years, found no consistent deviations from the normal average growth.

In regard to weight, Fischer *et al.*[6] found that there was a tendency for the boys to be underweight and for the girls to be overweight, especially during the years of puberty. They felt that since the caloric intake, according to their estimation, was similar, the greater physical activity of boys may explain the

difference in weights in the sexes. White[5] found that higher grades of overweight are limited to the girls and that the question arises whether this may not be the result of either (1) overnutrition, (2) an accentuation of a normal physiologic gain in weight which takes place at a certain age period, or (3) a manifestation of some continued endocrine disturbance.

In our studies we also found a tendency for the boys to be underweight and for the girls to be overweight. Even when the relationship of the individual's weight to height was determined it was found that this tendency is still evident.

Some observers have attempted to explain the relationship of growth in the diabetic child to the level of control of the diabetes. Jackson,[9] studying the relationship of growth to the level of control of the diabetes, found that it was difficult to demonstrate any definite pattern in those above the age of 10 years, while those diabetic children observed before 10 years of age showed less increase in height when under poor diabetic control. The children under good or excellent diabetic control have the opportunity of undergoing compensatory or accelerated growth.

Of course, in our group of subjects, we have no data indicating the type or degree of diabetic control that these children were under prior to coming to camp. During their camp stay, however, every attempt was made to maintain these children under as good diabetic control as possible. It is of interest to note also that Wagner, White, and Bogen[10] reported finding no definite relationship between retardation of growth and level of control of the disease. They also noted in studying the age-height relationship, using three different standards (Baldwin and Wood, Engelbach, and Meredith), that the diabetic children were slightly heavier for height than the nondiabetic.

Others have claimed[11] that more boys than girls tended to be below the minimum height standard. The weight of both sexes fell between the minimum and maximum standards. These results were obtained from studies on a group of 49 treated diabetic children.

Regarding the nutritional status of our children while at camp, a careful study of our figures shows that we tried to keep to the average caloric requirement for these boys and girls without being accused of practicing underfeeding or overfeeding. This of course is difficult to do when handling such a large group of children for such a limited period of time. Too frequent changes of diet and insulin allowance can upset the carbohydrate tolerance considerably and accomplish nothing more than adding further confusion to the situation. We were therefore particularly careful to avoid such results and changed the diet and insulin only when there was a definite indication.

The girls attending Camp NYDA seemed to show a greater degree of stability in their food requirements than the boys did. More than two-thirds of the girls remained on the same diet prescription throughout their camp stay, whereas almost half of the boys required changes in the prescription.

It is a common observation that the majority of nondiabetic children attending summer camps usually return showing some weight loss as the result of their increased physical activities while at camp. This occurs in spite of the rather high carbohydrate, high caloric food intake which they all usually receive. It is therefore interesting to note that our group did not fare badly in this respect. As noted in Table VIII, 40% of the boys and 37% of the girls ended up their camp stay showing a gain in weight. About the same percentage of weight loss was shown by both the boys and girls.

Our data on the insulin requirement of these children offer some interesting observations. Many of the children required a further increase in the insulin dosage over and above that which they were taking at home just prior to coming to camp. About 37% of both boys and girls (Table X) required this increase. This occurred in spite of the fact that they were going through a period of increased physical activity. Such data would lead us to suspect that the actual consumption of food at home was not always exactly that which was represented by the figures furnished to us on

the camper's application for admission to camp. This prompted us to undertake a careful analysis and calculation of such food consumption at home, to see how this compared with the figures furnished to us. These data will be presented separately at some future time.

An analysis of the insulin schedules used by the children both at home and while attending camp (Table IX) showed that about half of them were being controlled on NPH insulin. As previously mentioned, no attempt was made to change these children from one insulin to another. In a few instances, however, it was impossible to keep them well balanced on the type of insulin prescribed by their own physicians, and other routines had to be instituted. The insulin mixtures seemed to be the next most popular form of administration and accounted for 31% of the boy and 17.5% of the girl campers.

We were indeed very fortunate in that no serious complications were encountered in any of these children during their camp stay.

Summary and Conclusion

Comparative studies are presented with respect to weight, height, and relationship of weight to height, for 155 diabetic children attending Camp NYDA, during the summer of 1951. Similar studies of caloric intake are included.

In the boys' group there was a slight tendency to overheight and underweight. In the girls' group there was the same tendency to slight overheight but a rather definite and considerable tendency to overweight. Almost two-thirds of our girls' group were overweight.

At the end of their camp stay 40% of the boys showed a gain in weight as compared to 46% who lost weight. Essentially the same proportions held true for the girls. Approximately 43% of the boys' group and 25% of the girls' group required an increase in their food allowance during their camp stay; only 2 of the boys and 4 of the girls had their food intake reduced.

In addition to the 30% reduction of insulin dosage at time of admission to camp, 17.5% of the boys required further reduction in their insulin dosage as compared to only 13.5% of the girls. On the other hand, about 37% of both boys and girls required an increase in their total insulin dosage above their original home insulin dose, in order to be maintained under good diabetic control. Half of the children entering Camp NYDA had been maintained on NPH insulin alone. Our experience with various insulin mixtures is described.

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Resumen

Estudios nutricionales de diabéticos juveniles asistiendo a un campo de verano

Se presentan estudios comparativos con respecto al peso, altura y relación del peso con la altura en 155 niños diabéticos que asistieron al campo NYDA durante el verano de 1951. Se incluyen estudios similares con respecto a la ingestión de calorías.

En el grupo de muchachos hubo una ligera tendencia tanto al aumento como a la dis-

minución de peso. En el grupo de las muchachas hubo asimismo una ligera tendencia a la disminución de peso, pero en cambio una tendencia definida y considerable al aumento de peso. Casi las dos terceras partes del grupo de muchachas tenían sobrepeso.

Al fin de su estadía en al campo, 40 por ciento de los muchachos habían aumentado de peso, en comparación con 46 por ciento que habían disminuido. Las mismas proporciones se encontraron en el grupo de muchachas. Aproximadamente el 43 por ciento de los muchachos y el 25 por ciento de las muchachas requirieron un aumento en la cantidad de alimentos durante su estadía en el campo; solamente a dos muchachos y a cuatro muchachas se les redujo la cantidad de alimentos.

Fuera de la reducción del 30 por ciento en la dosis de insulina al tiempo de ser admitidos al campo, 17,5 por ciento de los muchachos requirieron una reducción posterior en su dosis de insulina en comparación con 13,5 por ciento en el grupo de muchachas. Por otra parte, cerca del 34 por ciento tanto de muchachos como de muchachas necesitaron un aumento en la dosis total de insulina comparada con la que recibían en casa, con el objeto de mantenerles dentro de un buen control diabético. La mitad de los niños del campo NYDA fueron mantenidos solamente con insulina NPH. Se describe nuestra experiencia con las diferentes mezclas de insulina.

Utilization of Intravenously Injected FRUCTOSE *and* INVERT SUGAR *in* NORMAL HUMAN SUBJECTS

By IRVIN H. STRUB, M.D., WILLIAM R. BEST, CAPT., M.C., C. FRANK CONSOLAZIO, AND MORTON I. GROSSMAN, M.D., PH.D.

WITHIN recent years increasing recognition has been given to the importance of calories in the intravenous feeding of patients. This recognition arose from the finding that adequate caloric intake is required for optimal nitrogen utilization. Currently invert sugar, fructose, ethyl alcohol, and fat emulsions are being studied in various laboratories as intravenous aliments that may possess advantages over glucose in terms of the number of calories per unit time that can be administered.[1] The present study is concerned with the rate of utilization of fructose and invert sugar to assist in evaluating their possible superiority to glucose.

PLAN OF THE PRESENT STUDY

In the studies reported here, answers were sought to the following questions: (1) What is the pattern of tolerance, in terms of blood and urinary sugar levels, when fructose and invert sugar are given in amounts comparable to those which would be desirable in the treatment of patients with caloric depletion? Previous investigators, although they have used relatively high rates of infusion, have continued the infusions for only 1 to 1.5 hours, giving a maximum of 150 Gm. of sugar. (2) What are the comparative rates of utilization of fructose and invert sugar? None of the previous investigators has administered these substances to the same group of subjects at the same rates, so as to permit direct comparison. (3) What is the effect of simultaneous administration of fructose on glucose tolerance? As indicated above, studies in animals suggest that simultaneous administration of fructose improves glucose tolerance.

METHODS

Nine normal male subjects, ranging in age from 27 to 45 years, each received each of the following infusions on separate days: (1) 141 Gm. of glucose (1500 ml. of 10 per cent glucose in water), (2) 291 Gm. of fructose, and (3) 288 Gm. of invert sugar (the latter two were both in the form of 3000 ml. of 10 per cent solution in water).* The solutions were given at a constant rate over a 3-hour period with the subjects in the fasting state. Blood and urine collections were made just before, each hour during infusion, and for 2 hours after the infusions. Since invert sugar consists of equal parts of glucose and fructose, the rate of administration of glucose was the same in the glucose infusion as in the invert sugar infusion. This permitted an evaluation of the effect on glucose tolerance of simultaneous administration of fructose.

Total reducing substances in blood and urine were determined by the Nelson[2] modification of the Somogyi[3] method. Fructose determinations were done by the method of Roe.[4]

From the Medical Nutrition Laboratory, Chicago; an installation under the jurisdiction of the Surgeon General, U. S. Army.

The opinions expressed in this paper are those of the authors and do not necessarily represent those of any governmental agency.

* 10 per cent glucose in distilled water was kindly supplied by Abbott Laboratories, North Chicago, Ill.; 10 per cent fructose and invert sugar in distilled water by Abbott Laboratories, North Chicago, Ill., and Baxter Laboratories, Morton Grove, Ill.

To provide a basis for calculating the blood and urinary levels of glucose and fructose, a study was made of the comparative reducing power of fructose and glucose in the Nelson method for total reducing substances and the amount of reaction produced by glucose in the Roe method for fructose. It was found that in the Nelson method, fructose produces 88 per cent as much reduction as does an equal amount of glucose. Four different samples of purified fructose,* dried for 48 hours in a vacuum desiccator, all gave the same result. Glucose was found to produce 2 per cent as much reaction in the Roe method for fructose as does an equal amount of fructose. Simultaneous equations were derived to permit calculation of the glucose and fructose content of samples from the results of the Nelson and Roe methods:

$$G_g = 1.018\ G_t - 0.896\ F_t$$
$$F_f = 1.018\ F_t - 0.0204\ G_t$$

where G_t = total concentration of reducing substance (uncorrected value of the Nelson method determination), G_g = that part of G_t due to glucose, F_t = uncorrected value of Roe method determination, F_f = that part of F_t due to fructose.†

For the calculation of the percentage urinary sugar loss the concentration of sugar in the solutions infused was determined by actual analysis, rather than using the values given on the labels. In the case of glucose, the U.S.P. 10 per cent solution is based on the hydrated form of glucose and represents about a 9.4 per cent solution of the unhydrated form. The percentage of sugar (calculated as the unhydrated form), in the solutions infused, as determined by chemical analysis, was found to be:

10 per cent Glucose	9.4 per cent
10 per cent Fructose	9.7 per cent
10 per cent Invert Sugar	
Glucose	4.8 per cent
Fructose	4.8 per cent

Therefore, 1500 ml. of 10 per cent glucose contained 141 Gm., 3000 ml. of 10 per cent fructose 291 Gm., and 3000 ml. of 10 per cent invert sugar 288 Gm.

Results

Figure 1a shows the blood glucose levels, urinary glucose output and urine volume after the administration of 141 Gm. of glucose. The values are the means for the nine subjects and the bars indicate the standard errors. The blood glucose, after reaching an early peak, steadily fell in spite of the continued infusion at a constant rate. Hypoglycemic levels occurred in all subjects following termination of the infusions. The peak of the urinary glucose output was during the second hour of infusion and the maximal diuresis was during the third hour.

Figure 1b shows the blood and urinary values following the administration of 291 Gm. of fructose. There was a slight initial rise in blood glucose followed by a progressive fall during the course of the infusion, thus showing the same general pattern as in the glucose infusion. After the infusion was stopped blood glucose fell to hypoglycemic levels. In contrast, however, the blood fructose level did not fall during the infusion but rose slightly and then fell rapidly when the infusion stopped. The urinary sugar was mainly fructose and the peak of output as well as the maximal diuresis was seen in the third hour.

In Figure 1c, the blood and urinary values after the administration of 288 Gm. of invert sugar are presented. Again a sharp peak in blood glucose occurred with a progressive fall despite the continued administration of the sugar. Blood fructose levels remained rather constant during the infusion but fell rapidly upon termination. Thus, during the second and third hours of the infusion the blood glucose level fell while the blood fructose remained constant, although both glucose and fructose were being infused at constant and equal rates. The urinary sugar was divided approximately

* Kindly supplied by Prof. M. Wolfrom, Ohio State University; Baxter Laboratories; U.S.D.A., Western Regional Research Laboratories; and Pfanstiehl Chemical Company.

† The method of derivation of these equations is presented in the Medical Nutrition Laboratory Report of this work.[28]

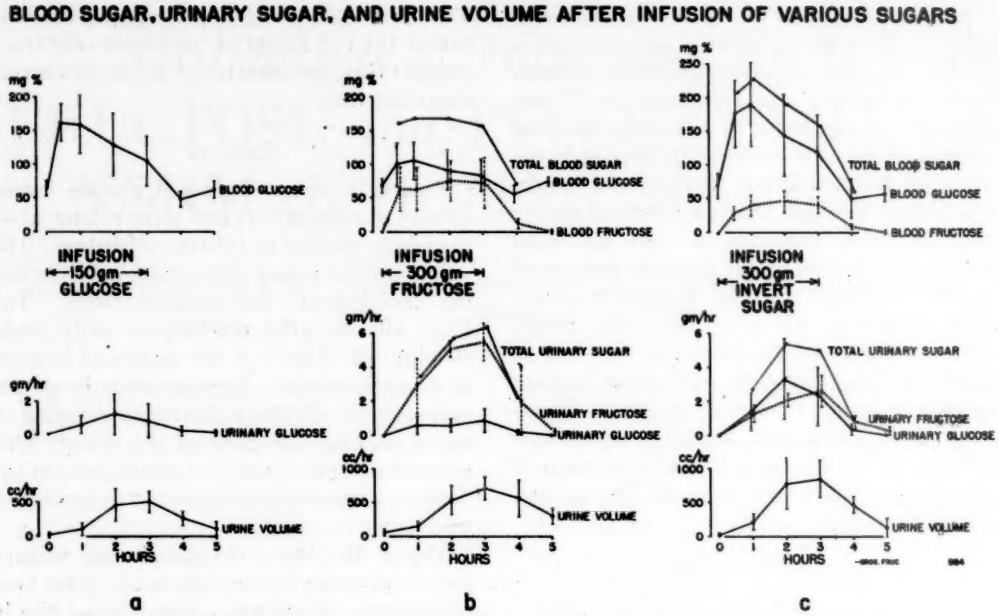

Fig. 1. Blood Sugar, Urinary Sugar, and Urine Volume After Infusion of Various Sugars.

equally between fructose and glucose and the maximal sugar output, as well as the maximal diuresis, occurred during the second and third hours of the infusion.

The mean values for the highest blood glucose, blood fructose, and total blood sugar are given in Figure 2. Blood glucose was highest with the infusion of invert sugar (198 mg. per cent) despite the fact that the rate of administration of glucose was the same as in the glucose infusion, in which the mean highest blood glucose value was 187 mg. per cent. During fructose administration the mean highest blood glucose was 118 mg. per cent.

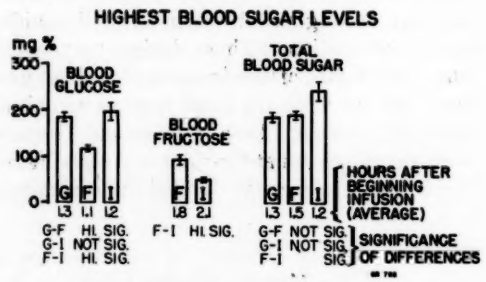

Fig. 2. Highest Blood Sugar Levels.

The mean highest concentration of fructose in the blood was almost twice as great during fructose infusion (92 mg. per cent) as during invert sugar infusion (51 mg. per cent), thus corresponding rather closely with the rate of administration of fructose, which was twice as great in the fructose infusion as in the invert sugar infusion. The peak values for blood fructose occurred somewhat later during the infusion than the peak values for glucose.

The mean highest total blood sugar was greatest with the invert sugar infusion (243 mg. per cent) as compared with the glucose infusion (187 mg. per cent) and the fructose infusion (191 mg. per cent).

The grams of sugar excreted in the urine in 5 hours, including the 3 hours of infusion and 2 postinfusion hours, are given in Figure 3. More glucose was excreted with invert sugar infusions (7.14 Gm.) than with glucose infusions (2.98 Gm.) even though glucose was given at the same rate in the two infusions. Glucose excretion with fructose infusion had a mean value of 2.21 Gm. Fructose excretion was approximately twice as great with fructose administration (15.84 Gm.) as with invert

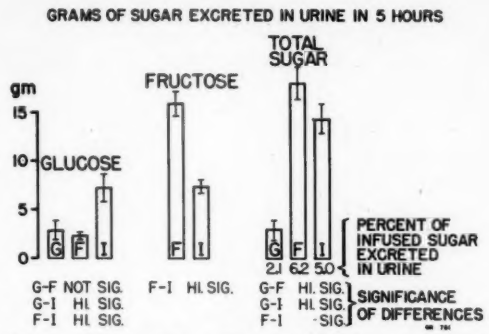

Fig. 3. Grams of Sugar Excreted in Urine in 5 Hours.

sugar administration (7.12 Gm.) and thus was proportional to the rate of administration of fructose because the rate of administration of fructose was twice as great in the fructose infusion as in invert sugar infusion. The total sugar excretion was greatest with fructose infusion (18.06 Gm.) and the amount lost with invert sugar (14.27 Gm.) was more than four times as great as with glucose administration (2.98 Gm.). The mean urinary sugar loss expressed as per cent of sugar infused was 2.12 per cent for glucose infusion, 6.21 per cent for fructose infusion and 4.96 per cent for invert sugar infusion. It will be noted that the urinary sugar loss was greater for fructose infusion than for invert sugar infusion, although the highest total blood sugar levels occurred with the invert sugar infusions.

The mean urine volume for 5 hours (3 hours of infusion plus 2 postinfusion hours) was 1493 ml. for glucose infusion, 2290 ml. for fructose infusion, and 2475 ml. for invert sugar infusion, representing 99, 76, and 83 per cent, respectively, of the volumes infused.

The maximal urinary fructose concentrations were considerably higher than the maximal urinary glucose concentrations. A graph of the data revealed that the slope of the curve relating blood fructose level to urinary fructose output is steeper than the corresponding curve for glucose. Fructose appears in the urine at very low blood fructose levels, confirming the well-known fact that the ability of the renal tubules to reabsorb fructose is much less than for glucose.[5]

During the infusion of the various solutions symptoms occurred in some of the subjects. With the infusion of the fructose solutions, six subjects developed symptoms of severe epigastric and substernal pain, as well as cramping sensations in the abdomen that in several instances radiated through to the back. These symptoms were so severe in one subject that on two occasions the infusion had to be discontinued and the results on this subject, therefore, are not included in the mean values. Milder symptoms of a similar character were seen in four subjects during the infusion of invert sugar. Only one subject noticed any symptoms during the infusion of glucose.

Discussion

These studies were not designed to compare tolerance for glucose with that for fructose and invert sugar, because glucose was given at a lower rate than the other two sugars. The previous studies[7–15] in which this direct comparison was made by the intravenous administration of glucose, fructose, and invert sugar at the same rates have, with one exception,[19] established that invert sugar and fructose produce lower total blood sugar levels and less urinary sugar loss than does glucose.

In the present study glucose was administered at a rate one-half as great as that used for fructose and invert sugar. This was done so that the rate of administration of glucose would be the same in the invert sugar infusion as in the glucose infusion. In the invert sugar infusion fructose was being given at the same rate as glucose. Thus a comparison could be made of the rate of utilization of glucose with and without simultaneous administration of an equal amount of fructose. This comparison revealed that the simultaneous administration of fructose with glucose resulted in higher blood and urinary glucose levels than with infusion alone. This is in contrast to animal studies in which fructose had been shown to improve glucose utilization.[16–18] However, the design of the animal experiments was quite different from the one we have used, and it is possible that under comparable conditions a similar effect might be demonstrated in human subjects.

In the present study larger total quantities of sugar were infused than in previous studies.

Two considerations directed this choice: (a) we wished to make the comparisons under conditions more comparable to the clinical situation in which infusions of large caloric equivalents are desired, and (b) since glucose shows a change in "tolerance" as the infusion is continued,[6] it was considered desirable to determine what influence this delayed effect would have on the comparative tolerance for fructose and invert sugar. Our results, as well as those of previous workers,[6] show that during a continuous infusion of glucose at a constant rate the blood glucose concentration reaches a peak and then progressively declines. This is attributed to the calling into play of mechanisms which increase the rate of removal of glucose from the blood and decrease hepatic discharge of glucose.[6] In contrast, the results of the present study show that the blood level of fructose reaches a maximum and then remains at a plateau level as long as the infusion is continued, indicating that no special mechanisms for fructose metabolism are mobilized as the result of fructose infusion.

The fact that the blood level of fructose remained relatively constant during the infusions of fructose and invert sugar indicates that once equilibrium had been established, the rate of removal of fructose from the blood stream was equal to the rate of infusion. Furthermore, since this plateau level of fructose was approximately twice as high with the fructose infusion as with the invert sugar infusion, and since the rate of fructose infusion was twice as fast in the former, it may be concluded that, within the range studied here, the rate of removal of fructose from the blood stream is proportional to the blood level, which in turn is proportional to the rate of infusion of fructose.

Weinstein[7] found that invert sugar given at a rate of 1.5 Gm. per Kg. per hour produced no more urinary sugar loss than glucose given at a rate of 0.75 Gm. per Kg. per hour. Our rates of administration of these sugars were similar to those of Weinstein, but we found that the mean urinary loss with invert sugar (5.0 per cent of infused sugar) was distinctly greater than with glucose (2.1 per cent of infused sugar). The total quantities of sugar infused were 3 times as great in our studies as in Weinstein's. Also, we used normal subjects, whereas those in Weinstein's series were patients with chronic illnesses. The work of Lawton *et al.*[12] suggests that in debilitated patients the tolerance for glucose is depressed more than that for invert sugar. Drucker *et al.*[20] have also found that in patients in the early postoperative state or ill with acute febrile diseases tolerance for glucose is impaired, whereas tolerance for fructose is not. This, together with the studies on fructose in diabetics,[21] suggests that under conditions in which glucose tolerance is impaired (e.g. "stress" and diabetes), tolerance for fructose may not be impaired.

Fructose infusions resulted in a distinctly lower elevation of total blood sugar than did invert sugar infusions, but the urinary sugar loss was slightly greater with the fructose infusion. The slightly higher urinary sugar loss of fructose as compared with invert sugar (3.8 Gm.), although statistically significant, is unimportant in terms of the additional caloric value of the sugar retained (14 calories).

Subjective symptoms such as were observed in some of our subjects during the infusions have been reported by only one other group of investigators.[13] The mechanism of production of these symptoms is not apparent.

More complete details of this study are presented in the laboratory report which has been published.[22]

Summary and Conclusions

Nine normal male subjects each received the following intravenous infusions lasting 3 hours each on 3 separate days: 141 Gm. of glucose, 291 Gm. of fructose, and 288 Gm. of invert sugar. The mean highest total blood sugar concentrations were 187 mg. per cent for the glucose infusion, 191 mg. per cent for the fructose infusion, and 242 mg. per cent for the invert sugar infusion. The urinary loss of total sugar (glucose plus fructose), expressed as per cent of sugar infused, was 2.1 per cent for glucose infusion, 6.2 per cent for fructose infusion, and 5.0 per cent for invert sugar infusion. Although under the conditions of this study it was found that in normal subjects the

percentage urinary loss is slightly greater for fructose infusions than for invert sugar infusions, there is a possibility that fructose might have specific advantages, other than providing calories, in certain clinical conditions because of its distinctive metabolic effects.

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Resumen

Utilización de la fructuosa y del azúcar invertido administrado por vía endovenosa en individuos normales

Cada uno de nueve hombres normales recibieron las siguientes infusiones intravenosas de tres horas de duración cada una en tres diferentes días: 141 gm. de glucosa, 291 gm. de fructuosa, y 288 gm. de azúcar invertido. Los niveles máximos de azúcar en la sangre fueron 187 mg. por ciento con la infusión de glucosa, 191 mg. con la de fructuosa, y 242 con la de azúcar invertido. La pérdida urinaria de azúcar total (glucosa + fructuosa) expresada como un porcentaje del azúcar inyectado fué 2,1 por ciento con la infusión de glucosa, 6,2 por ciento con la de fructuosa, y 5,0 por ciento para la de azúcar invertido. Aunque bajo las condiciones de este estudio se encontró que en sujetos normales el porcentaje de pérdida urinaria es ligeramente mayor con las infusiones de fructuosa que con las de azúcar invertido, existe la posibilidad de que la fructuosa tenga ventajas específicas en ciertas condiciones clínicas debido a sus característicos efectos metabólicos.

HEMOGLOBIN *Level and* DIETARY INTAKE *of Adults*

By LEONORA MIRONE, PH.D.*

SINCE THE Second World War nutrition programs have received increased emphasis throughout the United States. Because nutrition programs similar to those in other sections of the country were activated in the South, and because of the commonly held belief that hemoglobin levels are low and dietary habits poor in this region, it appeared that a hemoglobin level and dietary intake survey would be of value in pointing out the extent of the nutritional problem which might need greater study.

EXPERIMENTAL PROCEDURE

A sample of capillary blood for hemoglobin was obtained from 535 adults by pricking the finger of healthy volunteers with a spring lancet. The subjects were not examined clinically and the adjective "healthy" was used to denote that the participants showed no symptoms of illness and that they considered themselves healthy. The hemoglobin was determined by the oxyhemoglobin method;[1] the calibration factor was obtained by the Ponder[2] modification of the Wong Method. Two 0.02 ml. samples of blood were taken in calibrated pipettes. The blood was added to 5.0 ml. of 0.007 *N* NH_3 (0.04 ml. ammonia solution, sp. gr. 0.88, to 100 ml. with distilled water). Duplicate readings were made in a Klett-Summerson photoelectric colorimeter and the average of the two readings, agreeing within 0.5 Gm., was recorded for each sample.

The participants, residents of Georgia, were instructed to record the food intake on the United States Public Diet Record Form.[3] Food Value Tables for Calculation of Diet Records[4] and Taylor's[5] Food Tables were used to calculate the calories, animal protein, vegetable protein, fat, carbohydrate, calcium, phosphorus, iron, thiamine, riboflavin, niacin, and ascorbic acid intake for each individual. One hundred and thirty-nine men and 396 women volunteered to participate in the study.

From the Nutrition Department, School of Home Economics, University of Georgia, Athens, Ga.

* Associate Professor of Nutrition Research.

RESULTS AND DISCUSSION

Hemoglobin

The mean weight, height, age, and hemoglobin level for the men and women is shown in Table I. The average hemoglobin concentration for the men was comparable to that reported by Andresen and Mugrage[6] for men in Colorado; Heilmeyer and Hausold,[7] for men in Germany; and Jenkins and Don[8] for men in England. Likewise, the average hemoglobin concentration for the women was comparable to that reported by Osgood[9] for women in Oregon; Gargiulo,[10] for women in Argentina; Jenkins and Don,[8] for women in England; and Sankaran and Rajagopal,[11] for women in India. It would appear, therefore, that the average hemoglobin values for men and women in Georgia are in accordance with averages reported in other parts of the world.

Weight

Since weight in relation to age, height, and sex has long been held to be one indication of nutritional status, it appeared of interest to investigate whether underweight was associated with low hemoglobin levels. The percentage of underweight or overweight for each participant was calculated from the tables published by the Metropolitan Life Insurance Company.[12] The subjects were classified into 3 groups, namely: those 10 per cent or more underweight, those within 10 per cent of the normal weight, and those 10 per cent or more overweight, according to these criteria. As

TABLE I

Average Mean Weight, Height, Age, and Hemoglobin Level

Subjects	Weight	Height	Age	Hemoglobin	
				Range	Average
	lb.	*in.*	*yr.*	*Gm./100 ml.*	*Gm./100 ml.*
Men	164.5	70.1	28.8	13.04 – 18.23	16.13 ± 0.09
Women	126.2	64.1	27.1	10.39 – 16.83	13.99 ± 0.05

shown in Table II, underweight occurred at all hemoglobin levels, and there did not appear to be a close relationship between weight and hemoglobin values. Thus, it appears that underweight is not necessarily associated with low hemoglobin values. In a similar comparison study, Sheets and Barrentine[13] found no association between underweight and low hemoglobin values. Noteworthy is the fact that 23.8 per cent of the men were overweight as compared to only 9.1 per cent of the women. The proportion of overweight men in this study was significantly high. Thus, it indicated a need for stressing the hazards associated with overweight in nutrition programs.

Dietary Intake

The mean calorie, protein, carbohydrate, and fat intake of the participants is shown in Table III. The mean caloric intake of 2817 for men and 2081 for women was not significantly different from the Recommended Allowances of the National Research Council.

It was not surprising to find that the mean total protein intake for men was 96 Gm., with an average of 68.8 per cent of the total protein in the form of protein of animal origin. Stare and Davidson[14] reported that before rationing of food in the Second World War, it was not uncommon for persons to ingest daily 150 Gm. of protein chiefly of animal origin. Likewise, Cuthbertson[15] reported that for men the average protein intake varied from 30 to 121 Gm., with 68.5 per cent of the total protein coming from animal sources. The percentage of protein of animal origin to the total protein for women was similar to that of the men, namely 68.1 per cent.

Although the National Research Council does not specify the recommended dietary allowance for carbohydrate and fat, it is customary in planning diets to allow 50 to 60 per

TABLE II

Relationship between Hemoglobin Values and Weight

Hemoglobin	Subjects		Underweight, 10% and over		Normal weight		Overweight, 10% and over	
	No.	%	No.	%	No.	%	No.	%
Gm./100 ml.								
				Men				
13.00–14.49	8	7.1	2	25.0	5	62.5	1	12.5
14.50–16.49	73	51.8	14	19.2	43	58.9	16	21.9
16.50–18.49	58	41.1	6	10.3	36	62.1	16	27.6
TOTAL	139	100.0	22		84		33	
AVERAGE				15.8		60.4		23.8
				Women				
10.00–12.99	59	14.9	27	45.8	27	45.8	5	9.6
13.00–13.99	134	33.8	45	33.6	81	60.4	8	6.0
14.00–14.99	147	37.1	43	29.3	91	61.9	13	8.8
15.00–16.99	56	14.2	13	23.2	33	58.9	10	17.9
TOTAL	396	100.0	128		232		36	
AVERAGE				32.3		58.6		9.1

TABLE III

Mean Calorie, Protein, Carbohydrate, and Fat Intake

	Calorie	Animal Protein	Vegetable Protein	Total Protein	Carbohydrate	Fat
			Men			
Recommended allowances	3000	—	—	70	—	—
Mean intake, Gm.	2817	66	30	96	309	133
Standard error of mean	69.78	2.21	0.98	2.37	10.10	3.80
Standard deviation	823	26	12	28	119	45
Intake as calories		264	120	384	1236	1197
Intake as per cent of total calories		9.38	4.26	13.64	43.88	42.49
			Women			
Recommended allowances	2400	—	—	60	—	—
Mean intake, Gm.	2081	47	22	69	224	101
Standard error of mean	29.06	0.79	0.40	0.94	3.57	1.68
Standard deviation	578	16	8.0	19	71	33
Intake as calories		188	88	276	896	909
Intake as per cent of total calories		9.03	4.23	13.26	43.06	43.68

TABLE IV

Mean Mineral and Vitamin Intake

	Calcium	Phosphorus	Iron	Thiamine	Riboflavin	Niacin	Ascorbic Acid
	Gm.	*Gm.*	*mg.*	*mg.*	*mg.*	*mg.*	*mg.*
			Men				
Recommended allowance	1.0	—	12	1.5	1.8	15	75
Mean intake	1.09	1.65	16.82	1.69	2.28	17	96
Standard error of mean	0.05	0.04	0.43	0.05	0.08	1.76	15.60
Standard deviation	0.65	0.57	5.07	0.62	1.04	6.59	58.19
			Women				
Recommended allowances	1.0	—	12	1.2	1.5	12	70
Mean intake	0.82	1.2	12.2	1.2	1.6	12.1	84
Standard error of mean	0.02	0.02	0.19	0.04	0.05	0.21	2.72
Standard deviation	0.37	0.37	3.77	0.79	0.95	4.21	54.03

cent of the total calories from carbohydrate sources and 25 to 35 per cent from fat sources. As shown in Table III, the percentages of carbohydrate and fat consumed by the subjects are about equal, and both are higher than 40 per cent. This raises the question as to what role, if any, the equal ratio of fat and carbohydrate plays in obesity. Is fat *per se* or the origin of the fat (animal or plant) the more important contributing factor in obesity? Does the human organism metabolize and store fat of animal and of plant origin in the same manner? At present we cannot answer these questions, but it is hoped that future research will elucidate these problems.

It may be seen in Table IV that the mineral and vitamin intakes were well within the recommended allowances, with the exception of calcium. In the case of the men the calcium recommendations were just met, but among the women the calcium intake was somewhat lower than the recommended allowance. This finding is in agreement with Maynard's[16] belief that calcium may be deficient in many United States dietaries. However, recent, work appears to indicate that the calcium requirement may have been set too high.

Summary

A survey of 535 "healthy" adults in Georgia was made. The average hemoglobin level for the 139 men and 396 women was 16.13 ± 0.09 Gm. and 13.99 ± 0.05 Gm. per 100 ml. of blood, respectively. These values are well within the normal accepted standard for adults.

No close relationship was found between the

overweight and underweight distribution and hemoglobin levels. Therefore, it would appear that underweight is not necessarily associated with low hemoglobin values.

The calorie intake of this sample was not significantly different from the Recommended Allowance of the National Research Council. The protein intake was above the recommended allowance for both men and women and about two thirds of the total protein was of animal origin. The fat intake was high; over 40 per cent of the calories were derived from fat. This may indicate a very important factor in obesity. Curiously, 23.8 per cent of the men and only 9.1 per cent of the women were overweight. The mineral and vitamin intakes were well within the recommended allowance, with the possible exception of calcium in the case of the women.

The dangers associated with obesity and the provision for high nutritive diets of low caloric value are the factors to be stressed in nutrition education programs.

Acknowledgments

I am grateful to Miss E. Merle Wade, Mr. John J. Donovan, Jr., and Miss A. Marie Townsend for technical assistance.

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Resumen

Nivel de hemoglobina y dieta en los adultos

En Georgia se hizo un estudio de 535 adultos "saludables." El nivel promedio de hemoglobina en 139 hombres y en 396 mujeres fué 16,13 ± 0,09 y 13,99 ± 0,05 gm. por 100 ml. de sangre, respectivamente. Estos niveles se encuentran dentro de los límites normales del standard aceptado para adultos. No se encontró relación directa de los niveles de hemoglobina con el peso del individuo. Por lo tanto, parece que la disminución de peso no va necesariamente asociada con niveles bajos de hemoglobina.

La ingestión calórica de este grupo no fué significantemente diferente de la cantidad recomendada por el Consejo Nacional de Investigación. La ingestión de proteínas fué mayor que la cantidad recomendada tanto en hombres como en mujeres y cerca de las dos terceras partes de proteína fué de origen animal. La ingestión de grasa fué elevada; más del 40 por ciento de las calorías provenían de las grasas. Este puede constituir un factor muy importante en la obesidad. Singularmente, 23,8 por ciento de los hombres exhibían

sobrepeso, observandose este hecho en solo 9,1 por ciento de las mujeres. La ingestión de vitaminas y minerales estaba dentro de las cantidades recomendadas, con la posible excepción del calcio en el caso de las mujeres.

Los peligros asociados con la obesidad y la provisión de dietas altamente nutritivas de bajo valor calórico son los factores en los cuales debe ponerse énfasis en los programas educativos nutricionales.

Doctors and Dignity

"We become more conscious of our dignity as we grow older. Not that I think we have more real dignity now. In fact, we may have less of it in our character and thoughts since we joined in the battle of existence than we had in the fellowship of youth. Whether this is so or not, we certainly regard good lusty humour as unbecoming on important occasions, and there are many occasions which we consider important—or at any rate we feel important on so many occasions. Perhaps this is as it should be—although I do think that the wise clown has as much dignity as the sombre fool; but feeling ourselves important so often, we are leaving humour out of our lives more and more, and I believe greatly to our detriment."
—W. J. Saxton in an Address to the Queensland Branch of the British Medical Association. *The Medical Journal of Australia* II (15): 553–554, 1953.

Old Saying—New Meaning

"The old phrase of derision, 'He has a fat chance,' has become applicable with striking reality to the twenty-five million members of our community who are overweight and are, therefore, *poorly* fed."
—Charles Glen King. *Journal of the American Dietetic Association* 30: 15, 1954

Editorial

One Year Old

With this issue, the JOURNAL OF CLINICAL NUTRITION begins its second year of publication. We who have been connected with the JOURNAL are more than gratified by the reception it has received in the hands of our public. This has been reflected in the ever-increasing subscription lists, the growing group of organizations which advertise in its pages and, particularly, in the high quality of manuscripts submitted for publication. These all indicate, we believe, that the JOURNAL is furnishing an important service to the medical profession both here and abroad.

To our many friends and well-wishers who have offered kind criticisms, to our loyal readers and to our past, present, and future contributors go our heartfelt thanks and a pledge to continue our best efforts to make this JOURNAL—the only one of its kind—fulfill its objective: "the reporting of the practical application of our newer knowledge of nutrition."

—THE EDITORS

Nobel Prize 1953

To those interested in metabolism and nutrition, it will not come as a surprise that the 1953 Nobel Prize in Physiology and Medicine has been awarded to two outstanding biochemists, Professor H. A. Krebs, now at the University of Sheffield, and Professor F. Lipmann, now at the Massachusetts General Hospital, who richly deserve this honor. The work of both these investigators in explaining, in part at least, the hidden mysteries of the biochemical processes we know as *life* is widespread in its application.

Lipmann and his group showed the cardinal position of "active acetate"—acetyl co-enzyme A—in intermediary metabolism of fat, carbohydrate, and protein. It is significant that pantothenic acid is part of the co-enzyme A structure.

Krebs, over the years, has clarified one of the most complex and obscure of all physiologic activities—the enzymatic transfer of energy at the cellular level. The "Krebs Cycle" was a major step forward in our understanding of the ultimate breakdown of carbohydrate (and other substances) to carbon dioxide.

These awards again emphasize how great has been the recent accumulation of knowledge in the fields of nutrition, metabolism, and biochemistry. Since the Nobel Prizes were first awarded, in 1901, a large number of laureates have worked in these related fields. Earlier recipients include: Kossel, 1910, for studies on the chemical composition of cells; Hill and Meyerhof, in 1922, on muscle metabolism; Banting and MacLeod, 1923, on insulin; Eijkmann and Hopkins, 1929, on vitamins A and B; Minot, Murphy, and Whipple, 1934, on liver extract; Szent-Gyorgyi, 1937, on vitamins A and C; Dam and Doisy, 1943, on vitamin K; the Coris and Houssay, 1947, on carbohydrate metabolism. Proof indeed of the tremendous development in this phase of the biological sciences.

It is also to be noted that the two outstanding scientists just honored had found refuge and the freedom and opportunity to work in democratic countries; the intolerant persecution of these scientists left their fatherland the poorer, but the world the richer.

—S. O. WAIFE, M.D.

Vitamin B_6 in Human Nutrition

Among the vitamins of the B complex, B_6 has remained in relative obscurity because, during most of the twenty-year period since its discovery, its place in human nutrition remained unknown. Tentative reports of its value in the treatment of nausea of pregnancy and x-ray sickness were discounted as psychogenic, and the importance of evidence based on animal research tended to be minimized as inapplicable to man.

During the past two years, clinical evidence has accumulated to show beyond any reasonable doubt that B_6, a stepchild among vitamins, has a very real place in human nutrition. Credit for this discovery belongs to L. Emmett Holt and co-workers,[1] who observed convulsions in one mentally retarded young infant and anemia in an older child—both restricted to a vitamin B_6-deficient diet. Both of these manifestations (which yielded quickly to administration of pyridoxine) had been observed previously in young animals.

Holt's isolated report might have failed to achieve general recognition and might have been dismissed as a fortuitious result of brain damage associated with mental deficiency, had it not been for a chain of events involving a popular infant food, liquid S-M-A.®

Reports of convulsive seizures in a very small percentage (about 3 to 5 per thousand) of very young infants on an unsupplemented diet of liquid S-M-A® appeared at first sporadically and in a limited area; then, as attention was directed to these cases, additional reports began to come from widely separated communities.

Despite the report of Holt which, by hindsight, should have explained easily the course of events, the finger of suspicion was not directed at vitamin B_6 deficiency until very recently.

False clues and factors, which should have been, at best, of merely contributory significance, were strewn all about. First reports centered about a drought area in Texas, where mineral-surcharged artesian well water, used as a diluent for liquid S-M-A®, seemed a logical clue; in a nearby community where the use of bottled water was the rule, there were no instances of convulsions. But when the suspected water was used to dilute powdered S-M-A®, convulsions never occurred.

Another scapegoat for the convulsions in some infants was the change which had been made in the character of the fat in S-M-A®, in order to achieve the lower intestinal pH characteristic of a human milk diet. It had been shown by Barbero *et al.*[2] that the composition of the fat was a major factor in predisposing the intestinal flora in favor of the acidophilic *Lactobacillus bifidus*—hence the incorporation of palm oil in S-M-A® fat.

A change in the fat of S-M-A®—then convulsions in infants. Suspicion, no matter how unfounded it subsequently proved to be, was too devastating to be ignored; so quickly, all the new-fat S-M-A® was recalled and the old-fat formula reinstated. But there never had been any trouble with powdered S-M-A®, and it had the same fat!

Extensive laboratory studies revealed no trace of toxic material to account for the convulsions in some infants. Good scientific sense demanded that a factor be found in liquid S-M-A® that did not occur in the powder that had the same ingredients except for water. The only difference was in the processing: the liquid product required a higher temperature of autoclaving. Heat processing of foods containing protein and sugar is a known cause of destruction of amino acids, vitamins, and of complex chemical changes involved in Maillard's browning reaction. What, then, was destroyed? If Holt's observations on one patient were correct, and the previous observations on animals were applicable to man, thermal destruction of vitamin B_6 might be the real culprit.

A microbiological study[3] of the vitamin B_6 content of various milk products was immediately arranged for, but without awaiting the outcome of this work, pyridoxine hydrochloride was immediately added to liquid S-M-A®.

This study of milk preparations disclosed or confirmed these facts:

1. Milk from any source contains three

kinds of vitamin B_6: pyridoxal, pyridoxamine, and pyridoxine. Among these the first two are very easily destroyed by heat, while pyridoxine is relatively heat-stable.

2. Because S-M-A®, as manufactured, has a lower content of whey-constituents and a protein level close to that of human milk, its pre-autoclaving vitamin B_6 content is rather low—a point that never had seemed to matter, since no human need for this vitamin had been recognized. The high autoclaving temperature necessary for liquid S-M-A® further reduced the natural vitamin B_6 content, most of which was heat-labile.

3. When pyridoxine, the heat-stable form of vitamin B_6 was added to liquid S-M-A® before autoclaving, as is now the practice, thermal destruction proved minimal, and even after terminal autoclaving the food has an adequate vitamin B_6 content.

Since this action was taken, not a single case of convulsions in infants connected with liquid S-M-A® containing B_6 has been reported.

The most dramatic and convincing evidence that the convulsive syndrome under discussion was wholly due to pyridoxine deficiency was supplied by Dr. David B. Coursin of Lancaster, Pa., who, for a two and one-half hour period, recorded the brain waves of a young infant who had developed convulsions on an exclusive unsupplemented liquid S-M-A® diet and had gone into status epilepticus.

During the recording of the electroencephalogram, Dr. Coursin injected saline solution, which produced no change either in the EEG or in the patient's clinical condition. Finally, he injected 100 mg. pyridoxine intramuscularly, whereupon the pathologic brain wave pattern virtually disappeared within three minutes, while the infant patient's convulsions ceased and peaceful sleep ensued. Since then the patient has continued entirely well on an unsupplemented liquid S-M-A® diet for a period of two and one-half months, with an entirely normal mental and physical development.

Besides this striking report,[4] confirmatory observations have been received as private communications from more than twelve other pediatricians who volunteered to continue infants on liquid S-M-A® after convulsions developed, prescribing only small occasional injections of pyridoxine hydrochloride. Under this regimen, all the infants recovered promptly and enjoyed a perfectly normal development.

Even before such deficiencies were recognized, interesting evidence that a limited vitamin B_6 intake, sufficient to satisfy the needs of most infants, may produce striking deficiency symptoms in a few, had been supplied by Hunt, Stokes, McCrory and Stroud,[5] who aptly described this puzzling metabolic defect in one such infant as "B_6-dependency." In the case reported by them, a young infant who had been in a serious convulsive state for several weeks after birth responded dramatically to supplementary pyridoxine by mouth or by injection.

Recently Vilter[6] and co-workers reported observations in adults receiving a vitamin B_6 antimetabolite (desoxypyridoxine). Foremost among the clinical signs of B_6 deficiency seen in 34 of 50 patients participating in this experiment were (*a*) anorexia, nausea, listlessness; (*b*) seborrhea sicca-like dermatitis; (*c*) cheilosis and conjunctivitis; (*d*) glossitis; (*e*) pellagra-like dermatitis; and (*f*) polyneuritis. In addition, mild anemia and other changes in the blood picture were noted in some cases.

These observations, viewed in relation to one another, compellingly suggest these conclusions:

1. Vitamin B_6 is essential in human nutrition.

2. This need is amply satisfied by the diet usually avaliable to adults, children, and all but the youngest of infants.

3. The convulsive seizures that were seen in a few young infants on a marginal vitamin B_6 intake disappeared completely in all cases following administration of pyridoxine, either in the food or by injection. No permanent damage was found in treated cases.

Inevitably and regrettably, this vital new nutritional knowledge was acquired at the expense of some human suffering. This has been the fate of every major discovery in nutrition. —Paul György, M.D.

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Changing Minds and Diets

"Intelligence plays relatively little part in what we eat; hence, an intellectual approach has limited value, although it is the easiest to use. . . . One explains, one repeats for emphasis, one augments by demonstration, and, for good measure, one adds a written list for future reference. In this approach, the specialist tells the person what he should do and why. So far so good, but the 'teaching' needs to be preceded with the preparation of the patient for learning and must be followed by much more.

The patient must want to change his pattern of eating; he must want to change enough to offset the force of his habit of years. He must want to change the food pattern because he wants something more than he wants his customary food. He may want to get back to work, to feel like himself again, or to feel safe. He may accept change because there is something he wants to avoid. He may want to avoid pain, or weakness, or diabetic coma. What he is willing to do about his food when he is on his own will relate to his comprehension of the relation of food to what he wants to avoid or gain."

—Grace White. *Journal of the American Dietetic Association* 30: 25, 1954.

Dietotherapy

DIETS RESTRICTED IN FAT

By CORINNE ROBINSON*

THE FAT content of the normal diet may be modified both qualitatively and quantitatively. One or both of these changes may be desirable in order that the caloric intake may be increased or decreased, and that the kind and amount of fat ingested may be compatible with the efficiency of fat digestion. This article will be concerned with qualitative and quantitative fat restriction as it is usually applied in the dietary treatment of diseases of the gallbladder.

NORMAL DIETARY ALLOWANCES FOR FAT

The modification of the fat content of the diet will be more intelligently planned when one is aware of the many important functions of fat in normal nutrition. Voluntarily, people in the United States select diets in which 20 to 40 per cent of the calories come from fat. The fat available for consumption per capita per day in this country is approximately 140 Gm.

Fats, being the most concentrated source of calories in the diet, supply $2^1/_4$ times as many calories as do equivalent weights of protein and carbohydrate. Thus, a reduction of the fat content of the diet by 100 Gm. would necessitate the addition of 225 Gm. of carbohydrate and protein if the caloric level were to be kept constant. The bulk of the diet is thereby considerably increased and people who are ill may find it impossible to eat the additional amounts of food required to maintain caloric balance. One possibility often suggested to surmount the bulky diet is to include sugars such as glucose or lactose in fruit juices and prepared foods. This is an acceptable procedure for some patients, but not satisfactory for others.

* Head, Dept. Food and Nutrition, Drexel Institute of Technology, Philadelphia, Pa.

Fats contribute importantly to the satiety value of the diet. The sense of well-being experienced from this class of foodstuffs is no doubt the result of the longer time which fats remain in the stomach. This factor is at least one reason why calorically restricted diets which are moderate in fat content give promise of greater success for the correction of obesity than do isocaloric diets severely restricted in fat but providing greater amounts of bulk in the form of fruits and vegetables.

The flavors and odors of fat impart palatability to the diet not replaceable by other dietary constituents. The mouth-watering qualities of a steak well marbled with fat, the fine flavor of buttered vegetables, the piquancy of flavors blended in a salad dressing, the satisfying quality of butter with bread—all call forth feelings of pleasure. In times of scarcity when food must be rationed, people are willing to stand in long lines in order to get their "share" of fats.

Fats are sources of the essential fatty acids, but these substances can be obtained even in diets severely restricted in fat. Under experimental conditions healthy persons have been maintained without untoward symptoms on diets providing only 1 per cent of the calories from fat. However, it would be practically impossible to achieve acceptance of such extreme diets by ill people.

Fats are carriers of the fat-soluble vitamins. Diets in which whole milk, egg yolk, and cheese are omitted are correspondingly reduced in vitamin A content. This reduction is not corrected by the inclusion of yellow and green leafy vegetables in those situations where the ability of the body to convert carotene to vitamin A is diminished. Thus, severe restriction of dietary fat will necessitate the addition to the diet of supplementary vitamin A.

There is good reason to believe that some restriction of fat may be beneficial to many persons in that it may help to curtail the incidence of obesity. Nevertheless, in view of the important considerations noted above, it becomes essential in planning the fat-restricted diet to consider not only the qualitative and quantitative changes required, but also to consider the diet in all its aspects and the patient as an individual.

Dietary Sources of Fat

Approximately half of the fat in the average American diet is provided by the so-called "visible" fats. These include lard, butter, and plant oils from the cottonseed, soybean, corn, coconut, and peanut. The oils are used not only as such, but in the manufacture of hydrogenated fats and margarine under many brand names. Of these fats, butter and fortified margarine are the only ones which contain vitamin A—approximately 15,000 I.U. per pound.

Sources of the "invisible" fats include whole milk, whole milk cheeses, and cream; meat, poultry, and fish; egg yolk; nuts and cacao products; and there are small amounts of fat in grains and legumes.

Milk, cream, and cheese account for about one-fifth of the average daily fat intake. Whole milk is of relatively constant fat composition, varying from 3 to 4 per cent depending upon local regulations. Coffee cream contains about 18 per cent fat, and ice cream an average of 12 per cent fat. Hard cheese made from whole milk contains in excess of 30 per cent fat, but cottage cheese made from skim milk contains as little as 1 per cent fat.

Meat, poultry, and fish contribute approximately one-fifth of the daily fat in the diet. The average fat content of meat is about 15 to 20 per cent, but the range is wide. Very lean meats such as veal, liver, and turkey may contain as little as 6 per cent fat, while many pork products exceed 30 per cent fat.

All of the fat in the egg is concentrated in the yolk, each egg supplying about 6 Gm. The fat in the egg yolk is of special interest because it is associated with the most concentrated dietary source of cholesterol.

Of plant foods, nuts and chocolate are exceptionally high in fat, containing in excess of 50 per cent fat. Olives and avocados are likewise high in fat. On the other hand, cereal grains, fruits, and vegetables contain less than 2 per cent fat.

Normally, fats are almost completely digested and absorbed, the coefficient of digestibility being about 95 per cent. The rate of digestion is dependent upon the kind and amount of fat in the diet. Highly emulsified fats such as those in butter, cream, whole milk, and egg yolk are easily utilized, and moderate amounts are well tolerated even by most individuals in whom there is some interference with the flow of bile. On the other hand, the fats in fatty meats and fish and in fried foods retard the rate of digestion, and may be poorly tolerated by those with a faulty bile production or flow.

Restricted Fat Diet

The restricted fat diet used in diseases of the gallbladder should have the following characteristics: (1) nutrients provided at levels essential to maintain or restore normal nutrition; (2) fat restricted to a level compatible with adequate nutrition; (3) fats restricted to those which are highly emulsified and readily digested; and (4) foods bland in flavor and nondistending.

A fat restriction to approximately 60 Gm. daily can be achieved without compromising good nutrition. Some patients who require diets restricted in fat have a poor tolerance for strongly flavored vegetables, melons, legumes, and spicy foods. Others do not experience discomfort after eating such foods so that their inclusion or exclusion is a highly individual matter. One plan suitable for a fat-restricted diet is presented here:

RESTRICTED FAT DIET

Suggested basic foods	Household measure	Approximate weight, Gm.	Average fat content, Gm.
Milk	2 cups	480	18
Egg, whole	1	50	6
Lean meat, poultry, fish, or cottage cheese	5 ounces (raw wt.)	120 (cooked wt.)	17

Whole grain or enriched cereal	1/2 cup cooked or 3/4 cup dry	30 (dry)	1
Whole grain or enriched bread	3 slices	90	3
Potato, white or sweet	1–2 servings	150	Tr.
Green or yellow vegetable	1–2 servings	150	Tr.
Other vegetable	1 serving	100	Tr.
Fruit, including 1 citrus	3 servings	300	Tr.
Butter or margarine	3 teaspoons	15	12
TOTAL FAT			57

Nutritive value of basic list of foods: calories, 1475; protein, 75 Gm.; fat, 55 Gm.; carbohydrate, 170 Gm.; calcium, 0.9 Gm.; iron, 14 mg.; vitamin A, 12,500 I.U.; thiamine, 1.3 mg.; riboflavin, 2.0 mg.; niacin, 12.8 mg.; ascorbic acid, 140 mg.

The calorie level is increased or decreased by adjusting the amounts of bread and cereals, potato, sugars, and sweets. Desserts may be planned on the basis of the milk and egg allowance of the diet, and may include, in addition to fruit ices, gelatin desserts, milk puddings, and fruit whips made with egg white.

If severe fat restriction is necessary, the diet may be modified by substituting skim milk for whole milk, and omitting whole egg and butter or margarine. Such a diet requires supplementation with vitamin A whenever there may be a question of the conversion of carotene to vitamin A.

Additional protein may be provided by using nonfat milk solids, egg white, cottage cheese.

These foods are generally *contraindicated:*

High Fat Foods
- Chocolate
- Cheese except cottage cheese
- Cream
- Fatty meats or fish; bacon, pork, goose, duck, mackerel, sardines
- Fried or greasy foods: griddle cakes, doughnuts, potato chips
- Gravies and sauces
- Nuts; peanut butter
- Oils, cooking fats
- Rich desserts: pie, ice cream, cookies, cake except Angel Food, pastries
- Salad dressings, including mineral oil dressings.

Also omitted if not well tolerated:
- Strongly flavored vegetables: broccoli, Brussels sprouts, cabbage, cauliflower, cucumber, onions, peppers, radishes, turnips
- Legumes
- Melons
- Berries
- Spices

Meal plans should always be adapted to individual requirements. The following plan illustrates the use of the basic foods, but should not be construed as a fixed guide for the use of all persons.

SUGGESTED MEAL PATTERN	SAMPLE MENU
Breakfast	
Citrus fruit	Half grapefruit
Cereal	Wheat flakes with milk and sugar
Egg—1 only, not fried	Soft cooked egg, 1
Toast	Toast
Butter—1 teaspoon only	Butter, 1 teaspoon
Hot beverage with milk, sugar. *No cream*	Coffee, black or with milk, sugar
*Lunch or Supper**	
Clear soup, fat free, if desired	Boullion
Sandwich	Sandwich
Bread—2 slices	Wholewheat bread—2 slices
Butter—2 level tea spoons	Butter—2 teaspoons
Lean meat—2 ounces	Chicken—2 ounces (medium slice)
Raw vegetable	Lettuce
Fruit	Whole tomato
Milk—1 cup	Banana
Hot beverage, if desired	Milk
Dinner	
Meat, poultry, or fish, lean—3 oz.	Roast beef, lean
Potato or substitute	Steamed rice (no fat)
Vegetable, green or yellow	Green beans (no fat)
Salad, if none served at noon. (No oil dressing!)	Carrot, celery strips
Fruit or low fat dessert	Raspberry ice
Milk—1 cup, as beverage or in dessert	Milk
Hot beverage, if desired	Tea with lemon, sugar

* Planned as a lunch which might be carried to work, purchased at a lunch counter, or easily prepared in the home.

Nutrition News

☆ *News of activities in the field of clinical nutrition should be submitted to the Editorial Office of the* JOURNAL.

Third International Congress of Nutrition

Nutritionists from all over the world will gather in Amsterdam from September 13–17, 1954 for the Third International Congress of Nutrition, held under the auspices of the International Union of Nutrition Societies. Dr. B. C. P. Jansen, Professor of Physiological Chemistry at the University and Director of the Netherlands Institute of Nutrition, Amsterdam, will act as President.

Special emphasis will be given to symposia on "Nutrition and Disease" and "Food Additives," and the discussions will include: *Overnutrition and Disease, Nutrition and Liver Disease, Parenteral Nutrition, Nutrition and Psyche,* and *Non-nutrient Foreign Chemical Substances in Foods (Intentional Additives).*

The full text of the proceedings will be published in the Congress-book, edited by *Voeding,* the Dutch Journal of Nutrition.

Nutrition Fellowship

The National Vitamin Foundation (15 East 58th St., New York 22) has established a three-year $15,000 fellowship for postdoctorate training in nutrition to be given to a candidate holding a doctorate in medicine or in one of the biological sciences. Christened *The Russell M. Wilder Fellowship,* the new grant honors the former Director of the National Institute of Arthritis and Metabolic Diseases of the National Institutes of Health.

Drummond Memorial Fund

On the anniversary of Sir Jack Drummond's tragic death, his friends, in a spirit of admiration, loyalty, and enthusiasm undertook the establishment of a Memorial in his honor. The form of the Memorial now planned has a peculiarly strong appeal with reference to Sir Jack. To quote from Lord Woolton's statement of the plan:

"He had devoted twenty years to work in the field of experimental nutrition and the nation had begun to realize the immense importance of food in relation to health and the prevention of disease.

"During the 1939 war Drummond used this knowledge admirably in the interests of the nation. He applied himself with almost a crusading zeal to meeting the particular nutritional needs of the growing child, the expectant and nursing mother, and the sick. As a result we introduced, through the Ministry of Food, important measures that have had far-reaching consequences.

"This work ought not to be forgotten, and a committee has been formed, under my chairmanship, to ensure that his name and work may live. We have thought that the most suitable memorial would be to endow a Drummond Research Fellowship in this subject of nutrition. The Fellowship, which would cost about £25,000, would be administered by a body of University Trustees and be tenable in any university or appropriate research institution.

"We beg that all who share our sense of indebtedness to the work of Drummond, whether they be societies of various kinds, industrial organizations, or private people who feel grateful will subscribe generously to this appeal."

The committee formed initially in the United Kingdom to sponsor the Memorial consisted of Lord Woolton, Lord Horder, E. C. Dodds, Harold Hinsworth, Wm. Slater, Norman Wright, A. C. Chibnall, G. F. Morrison, F. G. Young, Ifor Evans, L. Anderson, H. J. Channon, Harry Jephcott, and Wilfred Vernon.

It is appropriate, also, to quote from Dr. H. J. Channon's tribute to his friend:

"Drummond's death leaves a gap such as is seldom left by the death of any one man. But it is also true to say that seldom has one man struck so vivid a flash of friendship, enthusiasm, and enterprise in all he met."

Knowing that friends of Sir Jack on this side of the Atlantic, who had the privilege of sharing in his friendship—and often in his work—will want to share in perpetuating memories of his scientific accomplishments and radiant personality, the following committee has joined in formulating this appeal for contributions to the Memorial honoring Sir Jack Drummond:

Charles H. Best	Karl E. Mason
R. Keith Cannan	L. A. Maynard
Hans T. Clarke	L. B. Pett
A. S. Cook	Wm. H. Sebrell, Jr.
Vincent du Vigneaud	Elmer L. Sevringhaus
E. C. Kendall	M. L. Tainter
C. G. King	John B. Youmans

Contributions may be made payable to the Drummond Memorial Fund and (to facilitate promptness and monetary exchange) forwarded to Professor L. A. Maynard, Cornell University, Ithaca, N. Y.

ESSAY CONTEST ON CLINICAL NUTRITION

The JOURNAL OF CLINICAL NUTRITION announces an essay contest open to the internes and residents of hospitals throughout the United States. This contest seeks to stimulate interest on the part of hospital medical staffs in clinical nutrition—with special emphasis on hospital aspects of nutrition. By directing the attention of the younger physician to this key subject, we believe the contest will serve the hospitals' interests, as well as provide our readers with even broader coverage of this important phase of the nutritional field.

Each paper will be carefully considered by the editorial board of the JOURNAL OF CLINICAL NUTRITION and will be judged solely on merit. Manuscripts must be received at the editorial office of the JOURNAL, 133 South 36th Street, Philadelphia 4, Pa., by July 1, 1954. Awards for the essay contest include $200 in prizes and one-year subscriptions to the first one hundred entrants. For further information, write to the Editor.

Nutrition Briefs

CURRENT OBSERVATIONS OF CLINICAL INTEREST

SOLUTIONS (10%) of honey and of dextrose were administered by gradual infusion to healthy subjects and patients with liver disease. Blood sugar curves revealed that the honey solution was much more rapidly utilized, and that dextrose utilization was definitely impaired in the patients with liver disease. This was not the case with levulose. The invert sugar content of honey probably explains its more efficient utilization in these patients.

H. Trautwein and H.-J. Grünefeld. *Ärzt. Forsch.* 7: 503, 1953.

SIX of 17 patients with trigeminal neuralgia obtained complete relief and two marked diminution of pain after receiving 50 μg. vitamin B_{12} twice daily for 10 days. The follow-up period was 2 to 8 months. Spontaneous remission, frequent in this condition, is rejected as a possible explanation of such a high incidence of improvement.

E. Alexander, Jr. and C. H. Davis, Jr. *North Carolina M. J.* 14: 206, 1953.

SCHOOL children in El Salvador and Guatemala (low to lower-middle economic classes) show a 2- to 4-year retardation in height, weight, and skeletal development when compared to United States school children. Their diet was found to be generally deficient in animal protein, vitamin A, riboflavin, and calcium. Daily supplementation with 20 μg. of vitamin B_{12} had no effect on weight; it did produce a height increase of less than 5 per cent.

N. S. Scrimshaw and M. A. Guzman. *Bol. ofic. sanit. panamer.* 34: 551, 1953.

LEARNING ability, as measured by mathematical tests, was said to be improved in both young and old persons by long-term administration of phosphorus (1.5 Gm. NaH_2PO_4 daily). After phosphorus administration was instituted, improvement continued throughout the training period and failures were rare.

R. Ehrenberg, H. Breitbach, and J. Schmier. *Naturwiss.* 40: 112, 1953.

THREE GRAMS of methionine daily for 6 weeks added to the usual diet had no effect on serum cholesterol or lipoprotein levels in 24 males with hypercholesteremia.

G. V. Mann, D. L. Farnsworth, and F. J. Stare. *N. Eng. J. Med.* 249: 1018, 1953.

SODIUM bicarbonate and magnesium trisilicate were introduced into the fasting stomachs of 16 patients, and fractional samples were analyzed for 2½ hours. Free acid reappeared as soon as the alkali had been neutralized or had left the stomach, and it did so in concentrations similar to those present before the alkalis were introduced. No evidence was found of a rebound secretion of acid within this period.

J. S. Staffurth. *Lancet* 2: 227, 1953.

FAILURE of intravenous iron to influence the anemia of patients with rheumatoid arthritis could not be predicted from the results of any of the usual investigations. Hemoglobin returned to within normal limits when one or more of the following were present: sedimentation rate below 30 mm. in 1 hour; microcytosis; gross hypochromasia, and raised total iron-binding capacity of the serum.

M. R. Jeffery. *Brit. M. J.* 2: 912, 1953.

RECENT ADVANCES IN EXPERIMENTAL NUTRITION

CARIES could be reduced in white rats on a cariogenic diet if gluten was substituted for part of the maize, but only if the gluten was given immediately after the weaning period, and if the parents of the experimental animals had not already received the cariogenic diet with or without gluten.

R. Luyken, L. Dalderup, and B. C. P. Jansen. *Intern. Ztschr. Vitaminforsch.* 25: 42, 1953.

A BEER extract (obtained from evaporation of a light Pilsener lager) inhibits the development of alimentary liver necrosis in young rats on experimental diets in which mushrooms are the protein source. Brewery sediment had previously been shown to give the same protection to the livers of young rats on diets deficient in sulfur-containing amino acids or vitamin E. In both cases, the factor or factors responsible for this protective effect are probably derived from the bitter principles of the hops.

H. Fink, J. Schlie, and U. Ruge. *Naturwissen.* 40: 171, 1953.

SUPPRESSION of folic acid alone from the diet of pregnant rats did not prevent normal embryonic development, nor did the addition to a complete synthetic diet of succinylsulfathiazole (which inhibits the intestinal flora and hence the bacterial production of folic acid). However, if succinylsulfathiazole was given to pregnant rats deprived of folic acid, there were serious repercussions on the fetus: either fetal resorption occurred, or else there were various deformities affecting the face, the body, and particularly the development of the eye.

A. Giroud, J. Lefebvres, and R. Dupuis. *Intern. Ztschr. Vitaminforsch.* 24: 420, 1952.

Nutritional Quotes

Caloric Chronology

"In 1910 in the average American diet, protein contributed about 12 per cent, fat 32 per cent, and carbohydrates 56 per cent of the total caloric intake. In 1948, the protein figure remained unaltered while the fat percentage increased (to 39 per cent) and carbohydrates decreased (49 per cent). Of particular interest are the data on the diet of the business and professional men, a group noted for a tendency toward coronary disease, for whom the calculations based on [Durant's] data yield a figure of 58 per cent of the calories being derived from fat. Their diet contrasts strikingly with the therapeutic regimen in use in the treatment of coronary disease in which the three basic types of food—protein, fat, and carbohydrates—provide 16, 14, and 70 per cent of the calories. Even should the data on the business and professional men prove to be an overestimate, there is little doubt that the *average* American diet has a very high fat content and that this fraction of the caloric intake has been rising steadily during the past fifty years."
—*Nutrition Reviews* 11: 294, 1953.

Waist Span and Life Span

"To try to evaluate the asset of a thin body in an experimental animal one study was completed in which all of the white rats were allowed to grow normally and to become as fat as they desired until middle age. Part of the animals were then kept thin by daily exercise, part were kept thin by restriction of calories and part were allowed to remain fat. Even starting in middle life the rats obliged to keep thin had the greater length of life. This indicates that even in the rat, which is little subject to cardiovascular disease or diabetes, a thin body is an asset in terms of life span."
—Clive M. McCay. *Gastroenterologia* 80: 197, 1953.

Fat and Its Repercussions

"Discovery of the specific steps by which simple and complex fats are built up and broken down has had great and immediate significance. One can better understand, for example, the manner in which intakes of sugar, protein, fat, and vitamins all must be considered in approaching the problems of excess calories, high or low blood cholesterol, and the risks of accelerating glandular imbalances and premature aging. These changes link our day-to-day food habits directly with five of the six top causes of death, and with many others of less finality in their consequence."
—Charles Glen King. *Journal of the American Dietetic Association* 30: 13, 1954.

The Lipid Problem

"Disturbance of lipid metabolism, in disease and in experimental animals, predisposes to atherosclerotic disease, but the metabolic theory of atherosclerosis has to face such facts as the one that not all persons with coronary artery disease have an elevated blood cholesterol level. It is not yet clear whether our understanding of this subject has been helped or further confused by reference to lipid molecules of different flotation rates, as determined by the ultracentrifuge."
—*Nutrition Reviews* 11: 293–294, 1953.

Cholesterol and Metabolic Upsets

"Why associate with hypercholesteremia certain metabolic disturbances such as diabetes mellitus and glomerular nephritis?

"We know, after all, that when there is a disturbance of metabolism, whether of cholesterol or other factors, there occurs a veritable complete upsetting of all the nutritional elements in general, a real anarchy of the carbohydrates, proteins, and lipids, while in normal nutrition these same elements live in the greatest harmony of association. It would be too much to believe, as certain authors pretend, that by reducing or cutting out of the daily diet too great a quantity of lipids rich in cholesterol, one would thus succeed in correcting all the evils attributable to the latter. This would be the equivalent of affirming that the majority of high cholesterol foods were harmful to our health. Which is false. Furthermore, the most fervent partisans of this theory, which supposes that the deposits of cholesterol found in the course of certain vessels are the sole causes of arteriosclerosis, have never been able to prove it seriously 'in vivo,' either physiologically or biochemically."
—R. Lachance. *Gaz. méd France* 60: 38, 1953.

Foods of the Fat

"Obesity is clearly a result of high caloric intake, coupled with a declining physical activity during the period of maturity. It is also very likely that there are qualitative differences in the diet. Actually, as far as the reviewer is aware, no comprehensive study of the diet consumed by obese individuals is available. This seems to be an important missing link in the argument about the role of dietary fat in the etiology of atherosclerotic disease."
—*Nutrition Reviews* 11: 294, 1953.

Reading the Scales

"While much remains to be done to elucidate the etiology, the association between a variety of 'degenerative' diseases and overweight is well established. Years ago this relationship was brought out in E. P. Joslin's comment that scales are to chronic disease what the thermometer is to acute illness."
—*Nutrition Reviews* 11: 292, 1953.

Defects of Obesity Statistics

"In the case of individuals 45 years of age or less applying for not more than a $2000 policy, no blood pressure measurement or urinalysis was required. Such individuals constituted a large percentage of the substandard policies issued during the years included in the study of Dublin and Marks, and a part of the excess mortality observed in their study may be an artifact. These individuals could have had high blood pressure, nephritis, or diabetes at the time of the application for life insurance. Furthermore, the weight was ordinarily *estimated,* not measured, by the examiner, and it appears that many of these individuals have received lower overweight ratings than their actual weight would have called for. These facts represent serious methodological limitations, and a call for a new study of the excess mortality because of *overweight alone* is fully justified. Such a study is needed as a guide for the underwriting of such risks in the future, as well as a means for a valid estimate of the medical hazards of overweight. The cases used for the study should be selected from a common baseline, including physical examination (with measured height and weight), blood pressure measurement, and urinalysis."

—*Nutrition Reviews* 11: 292–293, 1953.

Nutrition in Medical Education

"What other facilities for education in nutrition can be offered to medical students? In some teaching hospitals there may be special clinics and research units dealing with nutritional problems. The student may gain much from attendance at obesity clinics, special metabolic units, and antenatal clinics where instruction is given to mothers on how to feed themselves and their babies. These all have some contribution to make to the education of the student in nutrition, but it is the day-to-day presentation to the student by his regular clinical teachers of the feeding problems needing to be examined and solved as a routine for their general run of in- and out-patients that, I submit, will give the student the interest in, and respect for, nutritional knowledge able to stand him in good stead throughout his career as a practising doctor."

—S. J. Cowell. *Proceedings of the Nutrition Society* 12: 176, 1953.

Nutrition and Cellular Function

"Nutrition is perhaps the most complex field in medicine today. It involves much more than the so-called well-balanced diet. Many groups of people live on diets that are not balanced and are, furthermore, inadequate. It is surprising, nevertheless, but they do adapt themselves fairly well to this lower standard without clinical evidence of nutritional deficiency. However, this adaptation is imperfect, and such people are more vulnerable to the conditioning factors of nutrition than are those who have higher dietary standards. They will show signs of dietary deficiency more readily than better-nourished individuals when subjected to diseases which decrease absorption of nutrients, interfere with their utilization, or increase their requirements. All these factors essentially affect the metabolic mechanisms of the cell. This is the heart of the process of nutrition. Therein must be sought the answers to the riddle of nutritional influence on cellular function. Some nutrients are primarily essential for supplying energy, others are needed as building blocks for the general structure and the metabolic machinery of the cell, while still others are required for specialized functions such as light sensitivity or keratinization. Thus nutritional deficiency may affect generally cellular function and structural repair systems by blocking the supply of energy and of structural units and it may also interfere with some specific cellular activity."

—R. D. Griesemer, C. N. Frazier, and I. H. Blank. *Medicine* 32: 203, 1953.

Milk, Life, and Teeth

"Rats given no other food for the whole of life except pasteurized cow's milk have the same span of life as rats fed a complicated mixed diet. This indicates that milk probably has all essentials, such as vitamins, that will ever be discovered, at least for the rat. . . .

"Rats that are fed nothing but fluid milk for the whole of life have somewhat denser bones when they die in old age. They also have teeth without decay. This is the first experimental group of rats that has been observed in the course of twenty-five years in which no animal had a decayed tooth. From these results with milk diets, one has indications that both the teeth and bones can be modified by diet."

—Clive M. McCay. *Gastroenterologia* 80: 198, 199, 1953.

Soft Drinks and Soft Teeth

"In the course of one study with white rats covering the span of life after normal growth, variables were used to determine if the form of fluid and the amount of fluid ingested daily might modify the conditions of old age or the length of life. . . . Beverages commonly consumed by Americans were used for this study. They included water, milk, coffee, and a 10% sucrose solution to simulate the common soft drink. In the beginning one of the common cola beverages was used in this study but the molar teeth of the experimental rats were so badly eroded by the end of six months that the rats could not eat normally, so this experiment was terminated."

—Clive M. McCay. *Gastroenterologia* 80: 198, 1953.

Reviews of Recent Books

Peptic Ulcer by Lucian A. Smith, A.B., M.D., M.S. in Med., F.A.C.P., and Andrew B. Rivers, M.A., M.D., M.S. in Med., F.A.C.P., Appleton-Century-Crofts, Inc., New York, 1953, pp. 576, $12.50.

In the foreward of this book, Dr. George B. Eusterman properly points out the unique emphasis placed upon the symptom of pain by the authors. Throughout the book they stress the significance of variations in pain in diagnosis of ulcer and its complications, as well as in differential diagnosis. The authors also draw heavily upon the tremendous volume of material accumulated at the Mayo Foundation for their opinions and conclusions on the controversial aspects of the ulcer problem. Such material allows for excellent analysis of morbid anatomy, but one wishes that the authors had been as thorough in their presentation of the corresponding physiology and pathologic physiology. Practically no mention is made of the relationship of the endocrine system, particularly the pituitary-adrenal axis, to gastric function or pathology.

Although treatment of peptic ulcer and its complications is not standardized, the authors are at variance with majority opinion on certain points. Their basic ulcer diet of milk and cream contains only 60 Gm. of protein. They do not suggest additional protein supplements which, for a variety of reasons, have been found desirable in ulcer therapy. Their approach to the treatment of gastric ulcer is heavily weighted on the surgical side, even though an ever increasing number of internists and surgeons are advocating a suitable trial of medical management. Conservative management is recommended by the authors in the treatment of hemorrhage, but this reviewer feels that blood should be administered even before the "pulse rate exceeds 140 beats per minute or a systolic blood pressure of less than 80 mm. of mercury" is reached. Prevention of shock in the patient with hemorrhage is a basic concept of conservative management with which the authors agree. Although this text contains much valuable information, this reviewer feels that it is deficient in many important data available in recent years.

Handbook of Dietetics for Nurses by C. F. Harris, Baillière, Tindall and Cox, London, and The Williams & Wilkins Co., Baltimore, 1953, pp. 196, $4.00.

This book presents the essentials of normal nutrition and the principles of diet in disease in a remarkably compact, modified outline form. The text is clearly written and should be readily understood by the student nurse. The author is well qualified to present the subject matter from the standpoint of British food customs and of ration allowances.

Almost half of the book is concerned with normal nutrition and includes essential information pertaining to: classification, composition, and function of food constituents; metabolism of food; food allowances on the basis of the recommended dietary allowances of the National Research Council; a table of nutritive values of foods; characteristics of foods and principles of cookery together with basic recipes; feeding during pregnancy and lactation; feeding of infants and children.

The second part of the book relates to therapeutic diets in diseases of the alimentary tract, liver, gallbladder and biliary tract, kidneys and urinary tract, cardiovascular and nervous systems, in arthritis and gout, in diabetes mellitus, and in obesity and leanness.

The text includes specimen diets to illustrate the principles observed in the treatment of the various disease conditions. The nutritive value of most diets has been calculated, and recommendations are made for supplementation whenever the diet itself is not nutritively adequate.

It is to be regretted that the diets are not more closely integrated with the normal diet. Because diets are prescribed for specific diseases, there appears to be a larger number of diets than necessary. For example, there is one set of equivalents for the diabetic diet and another set for low calorie diets, whereas one set of equivalents might serve both diets.

Several items in this book will be of special interest to the reader in the United States. There is an enlightening comparison of hospital dietaries during the last 100 years from a London hospital. The gluten-free diet for celiac disease is described. Also included are lists for low potassium diets, low and high calcium diets.

This book can be recommended as a useful reference to the dietitian and physician in correlating British and American practices in dietetics. C.R.

Gourmet Cooking for Cardiac Diets by F. Field, The World Publishing Co., Cleveland, 1953, pp. 350, $3.50.

This book is intended to help the patient with cardiac disease to plan and prepare appetizing foods even though the diet may be severely restricted. A considerable number and variety of recipes for the low sodium diet are included, together with a smaller number of recipes for low calorie, low cholesterol, and

low purine diets. In addition, menu plans and details for the low sodium, low calorie, low fat, low cholesterol, and low purine diets are given.

The recipes include ingredients found in most American kitchens, together with many suggestions for herbs and flavorings which can be stocked and used to advantage. The directions are concisely given and easily followed. For the most part, family-size recipes are listed, but the number of portions should be carefully noted before preparation is started, inasmuch as the number of servings varies from one to eight. It would seem impractical to use family-size recipes whenever low sodium milk is required, since this product is too expensive for routine use.

Estimated caloric and sodium values are stated for one portion of each recipe, except for bread, in which case values are given per loaf. The computations are based on the use of milk in those prepared foods where milk, low sodium milk, or other liquid might be used.

The parts of the book which concern details of the various diets and menu plans must be used with considerable caution. They cannot be recommended as a blanket substitution for detailed dietary instruction by the physician or dietitian, inasmuch as this presentation is poorly organized, sometimes misleading, and occasionally incorrect. For example, on page 60, there is no discrimination between foods of negligible sodium content such as most fruits and vegetables, and those naturally containing moderate to high amounts of sodium such as meat, eggs, buttermilk. Ordinary lots of cottage cheese would be salted, while even unsalted cottage cheese would be used in limited amounts or even omitted on severely restricted diets.

On page 63 there is no valid reason to describe dietary sodium content in terms of table salt (400 mg. Na or 1/4 teaspoon of table salt). The patient is likely to relate such a statement to the amount of table salt he may use.

Mineral oil salad dressings are recommended for low calorie diets, a practice long frowned upon by nutrition and medical authorities. The Kempner rice diet is inadequately described, and its inclusion is therefore questioned. The relatively few recipes included for low cholesterol and low purine diets detract from the unity of the book and add little in terms of usefulness.

The author recommends that the patient use this book as a supplement to specific diet instructions given by the physician. If that advice is followed, and if the patient already has a thorough understanding of his diet and of the specific foods which may be used, the recipes can be helpful in achieving interesting meal variety. C.R.

Books received for review by the *Journal of Clinical Nutrition* are acknowledged in this column. As far as practicable those of special interest are selected, as space permits, for a more extensive review.

The Mechanisms of Disease by J. Stambul, Froben Press, Inc., Fort Pierce Beach, Fla., 1952, pp. 746, $15.00.

General Biochemistry by W. H. Peterson and F. M. Strong, Prentice-Hall, Inc., New York, 1953, pp. 469, $8.65.

Food for Life, edited by R. W. Gerard, The Univ. of Chicago Press, 1952, pp. 306, $4.75.

Abstracts of Current Literature

ABSTRACTERS

CHARLES R. SHUMAN, M.D., EDITOR

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H. A. ZINTEL, M.D., *Philadelphia*

PROTEINS AND AMINO ACIDS

The importance of protein in human nutrition is demonstrated clinically by the numerous complications which beset the patient in whom protein nutrition has not been well maintained. These complications include an increased morbidity and mortality following surgical procedures, and acute medical disorders. Much attention has been given to the problem of the availability of amino acids from various protein sources and of the influence of these dietary constituents upon the enzymatic machinery of the body. The availability of amino acids is controlled to a large extent by the function of the gastrointestinal tract. However, the form of protein used as food and its method of preparation affect also the liberation of amino acids within the alimentary tract.

Effect of Protein Depletion on the Transaminating Activities of Some Rat Organs. J. Awapara. *J. Biol. Chem.* 200: 537, 1953.

Using male rats of the Sprague-Dawley strain, experiments were devised to determine any alterations in both alanine and aspartic transaminase activities of livers from animals maintained on a protein-free diet, and to compare these probable changes with those observed in the accessory sex organs of the male rat following castration, or administration of estrogen. The data obtained support the concept that liver enzymes can be lost as a result of inanition.

Alanine-glutamic and aspartic-glutamic transaminases were measured in the liver, kidney, prostate, and seminal vesicles of rats maintained on diets which provided 25, 8, or 0 per cent protein, respectively. On the protein-free diet the livers of the rats lost about 50 per cent of their original alanine transaminase activity in about 4 days, while no changes took place in the activity of aspartic transaminase. There were significant losses in the activity of alanine and aspartic transaminases in the kidneys of the animals maintained on the 8 per cent protein diet, but no changes were observed in the activities of those enzymes in the kidneys from animals maintained on the protein-free diet. The accessory sex organs showed no definite alteration on any of the diets.—M. K. HORWITT

Enzymatic Liberation of Amino Acids from Different Proteins. A. E. Denton and C. A. Elvehjem. *J. Nutrition* 49: 221, 1953.

Each protein studied was subjected to hydrolysis by crystalline pepsin, followed by hydrolysis by preparations of defatted and desiccated whole pancreas and duodenal powder. Liberation of amino acids was followed by the nitrous micro-method of Van Slyke, by the manometric micro-ninhydrin procedure, and by microbiological assays. It was found that the rate and extent of liberation of amino acids from beef, casein, and zein, when measured chemically, were about the same, with beef being hydrolyzed slightly more rapidly than the other two proteins. Wide variations occurred in the liberation of amino acids from the proteins when measured microbiologically. However, it again appeared that beef was hydrolyzed slightly more rapidly than the other two proteins. Microbiologically available arginine seemed to be liberated from all proteins studied very rapidly during the pepsin stage of digestion.—B. SURE

Improvement in the Efficiency of the Proteins in Milled Wheat Flour with Lysine, Valine, Threonine and an Extract from Condensed Fish Solubles. B. Sure. *J. Nutrition* 50: 235, 1953.

A study was made, using the albino rat as the experimental animal, of the influence of additions of the amino acids, lysine, valine, and threonine, and an extract from condensed fish soluble, on the efficiency of the proteins in vitamin-enriched milled wheat flour. It was found that the additions of such micronutrients changed the protein efficiency ratio of the proteins in white flour from 0.68 to 3.11. On the basis of similar nitrogen intake, the basal diet, containing proteins derived from milled wheat, supplemented with lysine, valine, threonine, and an extract from condensed fish solubles, approximately equaled the biological value, from the standpoint of growth, of a ration containing proteins derived from dried nonfat milk solids.

Lysine and threonine were found to play a *specific* role in economy of food utilization, which was determined by controlled feeding experiments.

As little as 0.1 μg. of vitamin B_{12}/animal/day, supplementing the ration containing lysine, was followed by appreciable increases of body weight in male rats, during a 12-week experimental period, but no noteworthy increases in growth were observed in the female rats on the vitamin B_{12}-supplemented ration. The increased growth in the male rats was due largely to greater food consumption.—B. Sure

Methods for determining the biological value of protein have depended upon nitrogen balance studies and growth curves on selected diets. Recently a correlation has been made between the urinary creatinine excretion and the biological value of protein. Papers on these two subjects follow.

Correlation Between the Biological Value of Protein and the Percentage of Creatinine in the Urine. J. R. Murlin, A. D. Hayes, and K. Johnson. *J. Nutrition* 51: 149, 1953.

In a previous publication the authors reported on the high degree of correlation found in human subjects between the biological values and the urinary creatinine arising from the proteins fed. In this paper further evidence is presented of this relationship derived from exactly parallel procedures with 9 dogs. The authors maintain that the high degree of correlation between biological values and creatinine nitrogen percentages in the urines of the last days of any given period of protein ingestion entitles this constituent of urinary nitrogen to consideration as a base line of reference for the evaluation of protein. With a very poor protein the amount of nitrogen excreted in the urine is large; the creatinine portion of the total nitrogen, therefore, is a small percentage; and the reverse holds for a good protein. The correlations arrived at in these experiments lend themselves to prediction of biological values from creatinine nitrogen percentages.—B. Sure

Nitrogen Metabolism in West African Children. B. Bray. *Brit. J. Nutrition* 7: 3, 1953.

Very few nitrogen balance studies have been reported on human subjects whose diet is habitually on the margin between adequacy and starvation. The experiments described in this paper were performed in order to determine the nitrogen metabolism in African children and then, by comparison with American data, to ascertain whether there is any difference in nitrogen economy between individuals accustomed to a poor and to a full diet.

A series of nitrogen balances was carried out in the Gambia on 8 West African boys, aged 7 to 9 years. No consistent change in the balance of nitrogen metabolism was found after the elimination of the parasites *Ascaris lumbricoides* and *Ankylostoma duodenale*. The proportion of dietary nitrogen lost in the feces was higher than in American children of similar chronological age. The total urinary nitrogen was low compared with that of American children, with a lower proportion of urea and a higher proportion of ammonia. The reduced urinary nitrogen resulted in a larger retention on a smaller intake than in American children. Balance data confirmed clinical observations on retarded development. The reduced requirements of chronically malnourished Gambian children were satisfied by intakes smaller than those of American children of the same age. Retention of nitrogen was not accompanied by a corresponding increase in body-weight under the conditions of this test.—B. Sure

The relationship of amino acid intake and nitrogen balance has considerable significance, since it has been shown that a deficiency of a single essential amino acid may result in a negative nitrogen balance despite an adequate nitrogen intake. The following three papers discuss amino acid and nitrogen excretion in relationship to protein and amino acid content of the diet.

Amino Acid Intake and Nitrogen Balance of College Women. M. A. Wharton, D. Tyrrell, and M. B. Patton. *J. Am. Dietet. A.* 29: 573, 1953.

Because there are few data relating nitrogen balance to amino acid intake it seemed desirable to these authors to collect more information on the subject. Average nitrogen balance data and corresponding intakes of ten amino acids are reported for 18 college women in 99 balance periods. Samples of food, urine, and feces collected during a period of study of calcium metabolism were used. The diet was adequate in all nutrients except calcium of which 600 mg. per day were provided. The protein content varied from 57–76 Gm. daily and the caloric intake from 30–40 cal./Kg. A series of diets planned for 7-day periods provided varying levels of protein from common American foods. Each food was weighed for each subject. An adjustment period of one week preceded the 7-day collection period in all cases. (It was im-

possible to ascertain from the report the number of balance periods reported for each subject.)

The data were presented in three groups according to nitrogen intakes: group I received less than 1 Gm. protein per Kg. body weight; group II, 1–1.12 Gm. protein/Kg.; and group III, more than 1.12 Gm. protein/Kg. In group I, the women retained an average of 7.75 mg. nitrogen/Kg. body weight; in group II, 14.18 mg.; and in group III, 31.95 mg. These averages were significantly different by Fisher's "t" test. Nine of the 14 negative balances occurred in group I, 5 in group II, and none in group III. The intake of the amino acids studied did not appear to be limiting factors since in every case the ingestion of thiamine, valine, leucine, isoleucine, lysine, phenylalanine, and tryptophane was much greater than that recommended by Rose for young men. Methionine, when corrected for losses due to hydrolysis of the mixed dietary, was in most cases greater than Rose's minimum requirements. In the few cases when it was lower, there was no apparent relationship to nitrogen retention.

The regression of nitrogen balance per Kg. body weight on nitrogen intake predicts nitrogen equilibrium at 0.85 Gm. protein/Kg. body weight or for a 56-Kg. woman at an intake of 47.6 Gm. protein. This value is considerably greater than the minimum requirements observed by Hegsted *et al.* and Leitch and Duckworth. This the authors do not consider unexpected since the data herein reported contain relatively few negative balances. In the area studied, the nitrogen retention was in direct relationship to the nitrogen intake.

The reviewer believes it is possible that minimal values may not have been obtained because of the low calorie intake which resulted in an average weight loss of 3 pounds during the 8-week period. These data will be difficult for readers to interpret, due to lack of individual values and poverty of detail concerning conduct of the experiment.—J. M. Smith

Amino Acid Excretion on Different Protein Intakes. M. A. Wharton and M. B. Patton. *J. Am. Dietet. A.* 29: 762, 1953.

Urinary excretion of arginine, histidine, isoleucine, leucine, lysine, phenylalanine, threonine, and valine for 18 women during 99 nitrogen balance periods was independent of intake within the limits studied. This paper reports selected data from a study previously reported (see preceding abstract). The subjects, 18 women, were grouped into two groups according to their average nitrogen balance data so that group I each day had received an average of 148.0 mg. nitrogen per Kg. and group II, 196.0 mg. These levels were significantly different ($P = .01$), as was the difference in average nitrogen balance (+5.12 mg. and +32.17 mg. per Kg. for groups I and II respectively). The differences in average excretion of the eight amino acids were very small and were nonsignificant. There was great individual variation within both groups. Arginine and phenylalanine excretions showed less variation than the other six amino acids.

The differences in *total* amino acid intake of the two groups were significant only for leucine, lysine, and arginine. On the basis of intake *per unit of body weight,* differences were significant for arginine, histidine, isoleucine, leucine, lysine, phenylalanine, and valine ($P = .01$) and highly significant for threonine ($P = .05$).

The urinary excretion expressed as percentage of intake was very similar in the two groups. The excretions expressed in decreasing percentages were histidine, threonine, lysine, valine, phenylalanine, leucine, and isoleucine.—J. M. Smith

Nitrogen Balances, and Amino Acid Content of Self-Selected Diets of Women. M. S. Reynolds, M. F. Futrell, and C. A. Baumann. *J. Am. Dietet. A.* 29: 359, 1953.

This paper reports the nitrogen balances and amino acid content of the diets of 12 women living in their own homes and selecting their own food. The subjects ranged from 30 to 42 years of age, with one woman of 64. Each woman weighed and recorded all food eaten for 30 days. For two 5-day periods of that time, she supplied samples of her food for analysis. Excreta were collected. Nitrogen determinations were made on food and excreta and amino acid content of food analyzed. Data for 28 balance periods are presented. In 15 of these, subjects were losing nitrogen from 0.5 Gm.–3.4 Gm./day. Four-fifths of these negative balances occurred on daily protein intakes below 1.13 Gm./Kg. The lowest of 0.6 Gm./Kg. is well above that reported by other investigators as sufficient to support nitrogen equilibrium in adults under controlled laboratory conditions.

The authors studied the effect of calorie intake on nitrogen utilization by grouping the data according to increasing calorie intake. It was noted that nitrogen storage was observed in only 2 of 13 periods when energy intake was below 30 cal./Kg. Nitrogen storage occurred in 9 of 15 periods when energy intake was 30 cal./Kg. or above. Unfortunately, the protein intake rose as the calories rose, so that it is difficult to predict what might have been the critical level for calories if the nitrogen intake had remained constant throughout.

All essential amino acids except methionine were furnished in amounts equal to or in excess of the Rose minima. Supplementation of the diet of one subject by *dl*-methionine and by milk produced no improvement in negative nitrogen balance. The content of 18 amino acids of ten 5-day dietary periods revealed that glutamic acid is furnished most generously and cystine in lowest concentration. The authors emphasize that their data are not offered as a means of determining minimum requirements or of criticizing existing recommendations. The study seems rather to be descriptive of what may be the excretion and dietary pattern of women on freely chosen diets.

One wonders how widely these negative nitrogen balances occur and whether they may not occur in this type of study because women cut their customary intake during periods of observation or conserve on samples saved for analysis. A controlled laboratory study of the same women over a longer period would be of interest.—J. M. SMITH

The recent knowledge concerning the excretion of amino acids in various disease states is admirably summarized in the following paper.

The Clinical Significance of Aminoaciduria. I. B. Brick. *New England J. M.* 247: 635, 1952.

The normal plasma levels for amino acids vary from 3 to 6 mg. per 100 cc. These levels are little affected by the diet in the normal individual. Amino nitrogen in the urine constitutes 1 to 2 per cent of the total nitrogen. The level of urinary nitrogen tends to be proportional to the plasma level. There is competition for reabsorption of amino acids by the renal tubules.

Aminoaciduria results from: (1) elevated blood levels; (2) renal disease; (3) specific abnormalities of the reabsorbing mechanisms of the renal tubules. The latter may be associated with a generalized aminoaciduria or with a loss of specific amino acids.

The deToni-Fanconi syndrome represents an inherited condition characterized by aminoaciduria, peptiduria, glycosuria, and excessive urinary loss of inorganic phosphate. Clinically one notes vitamin D-resistant rickets or osteomalacia, acidosis, and sometimes cirrhosis and retinitis pigmentosa. The blood values for amino acids, glucose, and phosphorus tend to be normal.

In Wilson-Uzman disease, one notes involuntary movements, muscular rigidity, difficulty in articulation and deglutition, and signs and symptoms of liver disease. Pathologically one finds bilateral symmetrical degeneration of the lenticular and caudate nuclei and cirrhosis of the liver. Recently it has been noted that aminoaciduria invariably accompanies this syndrome and the findings indicate that this represents the primary defect.

Cystinuria is recognized by the formation of cystine stones. It is usually associated with excessive loss of other amino acids as well as cystine. In cystinosis, there is generalized deposition of cystine crystals throughout the tissues of the body. The latter condition is fatal at an early age.

Three abnormalities are associated with a disturbance in the metabolism of phenylalanine and tyrosine:

1. Alkaptonuria is characterized by an excretion of homogentisic acid in the urine. Such urine turns black or brown when alkaline or exposed to air. Homogentisic acid also reduces Benedict's solution. In the second or third decade, the disease may exhibit pigmentation of cartilages and other connective tissue from a blue pigment which is a polymer of homogentisic acid.

2. Phenylpyruvic oligophrenia results from a disturbance in formation of tyrosine from phenylalanine with consequent excretion of phenylpyruvic and phenylacetic acids. There is also an increased excretion of other amino acids. The disease is transmitted by a single recessive gene and is characterized by mental retardation and sometimes by pyramidal tract manifestations.

3. Tyrosinosis has been reported in only one patient. It is caused by inability to oxidize a derivative of tyrosine, phenylhydroxyphenylpyruvic acid which is excreted in the urine. The defect has little clinical significance.

In patients with liver disease, the urinary excretion of amino acid nitrogen is usually in the normal range, excepting only patients with acute yellow atrophy and terminal hepatic failure. In some of the milder forms of liver disease, there may be changes in the qualitative pattern of amino acid excretion. It has been suggested that some of the neurological manifestations of hepatic failure may be referable to abnormalities in amino acid metabolism. Uranium poisoning results in damage to the proximal convoluted tubule with increased aminoaciduria without elevated blood levels. Excessive vitamin D therapy produced a clinical picture similar to the deToni-Fanconi syndrome, which was reversible. Aminoaciduria may be found in patients with progressive muscular dystrophy and in galactosemia. Urinary and blood amino acid levels are affected by adrenocorticotropic hormone, cortisone, hypophysectomy, adrenalectomy, thyroidectomy, and thyroxine administration.

[The reviewer would like to call attention to the fact that other hormones, including insulin, epinephrine, and pituitary growth hormone, also affect the plasma amino levels.]—L. W. KINSELL

An interesting relationship between nitrogen fertilization of the soil and the protein content of corn has been demonstrated, indicating that the biological value of this vegetable protein can be enhanced by adequate soil treatment.

Amino Acid and Protein Content of Corn as Related to Variety and Nitrogen Fertilization. H. E. Sauberlich, W. Y. Chang, and W. D. Salmon. *J. Nutrition* 51: 241, 1953.

A series of 19 corn samples of different varieties was selected for this study. The samples were obtained from field plots receiving either high or low nitrogen fertilization. They were analyzed for protein and 18 amino acids. The results revealed that the nitrogen fertilization employed and the variety selected may influence considerably the protein and amino acid content of the corn kernel. The protein content of the samples ranged from 6.8 to 12.0 per cent. The amount of all the amino acids increased with an increase in the protein content of the corn. However, there were considerable differences in the

rate of increase among the individual amino acids. The results indicated that with the high protein corn samples a greater proportion of the protein was zein as compared to the low protein samples. Nitrogen fertilization increased the protein and amino acid content of corn significantly, with the increase apparently largely in the zein fraction. However, other proteins were also increased and this was reflected by the presence of greater amounts of lysine and tryptophane.—B. SURE

Protein requirements during pregnancy have been widely debated by physicians. Some obstetricians feel that the incidence of toxemia and the fetal mortality rates bear little relationship to protein intake unless clinical nutritional deficiencies are obvious. Other workers feel that these obstetrical complications occur with greater frequency in the presence of low protein intakes.

Importance of Protein in Maternal Diets: and a Charity House Survey. J. H. Ferguson and M. L. Hinson. *J. Louisiana State M. Soc.* 105: 18, 1953.

Diets of 100 women attending antepartum clinics at the New Orleans Charity Hospital were rated according to National Research Council recommended allowances for pregnancy. Not one woman got a rating of "excellent" and only one could be called "good." Diets of 88 per cent of the Negro women and of 74 per cent of the white women were "poor or very poor." In no case were NRC requirements met.

Since there have been many attempts to correlate a low protein diet with the toxemias of pregnancy, it is interesting to note that the incidence of toxemias at the institution where these dietary revelations were made is, in the authors' word, "extraordinary."

Another survey included 209 women attending antepartum clinics of the Tulane Service at the same hospital. Of these, 85 per cent were Negroes. Patients were chosen at random and a 24-hour diet history taken. Only 9 of the 209 women questioned (4 per cent) consumed the NRC recommended protein allowance of 85 Gm. Thirty (22 per cent) consumed less than 30 Gm., and 80 (38 per cent) less than 40 Gm. Median and mean protein intakes were both 45 Gm.

By NRC or any other standards, these diets were entirely inadequate. The only comparable survey the authors could discover was one made in rural Mississippi in 1910. Figures from Boston and New York hospitals are given by way of contrast. Whereas 72 per cent of the New Orleans Charity Hospital patients consumed less than 55 Gm. of protein, only 38 per cent of 216 women at Boston Lying-In Hospital had intakes so low. And while 50 per cent of the New Orleans group had less than 45 Gm., only 14 per cent of the Boston series ate this little protein. In the New York group, 22 per cent met the NRC requirement of 85 Gm., as compared to only 4 per cent of the New Orleans patients. The mean protein intake for the New York women was 67 Gm., compared to 45 Gm. for the New Orleans group.

The authors stress that the diet survey does more than illuminate the protein status of these women during pregnancy—it also reflects the daily amount of protein eaten by these same women, and probably their families, throughout their lifetime.

This survey throws into melancholy relief certain regional discrepancies which mar the picture of our national nutritional status. It indicates, too, that there has been little improvement in the diet of this particular population since last it was studied in 1945.—C.-J. HOWELL

Effects of Diet During Pregnancy on Mother and Child. H. Gounelle, A. François, and J. Billette. *Bull. Acad. nat. méd.* 27 & 28: 465, 1951.

From results of an inquiry carried out in 1949–50, it emerges that if, in general, the pregnant woman in Paris eats enough meat, she consumes an insufficient amount of dietary products, eggs, and fish. There is, for example, a certain relation between the amount of animal proteins in the diet and the red blood cell level of the future mother. The place of milk seems to be preponderant. Birth weight and growth curves are *clearly more favorable* among infants whose mothers had a diet especially rich in animal proteins—over 70 Gm. per day.—H. TEULON

Protein malnutrition is associated with physiological changes which affect the heart and circulation. Studies reported from Africa and elsewhere have described the alterations in cardiac function under the heading of "malnutrition heart disease." The following paper reports certain of these physiological alterations.

Contribution to Respiration and Circulation in Protein Deficiency and in the Recuperative Period. U. Wetzel. *D. Ztschr. f. Verdauungs- u. Stoffwechselkrankheiten* 12: 276, 1952.

More than 1110 persons with protein deficiency damage were studied from the standpoint of vital capacity. Before protein deficiency damage, these subjects had been in perfect health and able to work. It was found that vital capacity was decreased as compared to healthy subjects. After correction of the deficiency state, 910 of these subjects were followed during the recuperative state. Heart and circulation were investigated by cardiac function tests, electrocardiogram, or both. Tachycardia and bradycardia were rare, as compared with findings of protein deficiency damage. Hypotonia was seen more often, but disappeared with the passage of time. Some two-thirds of the subjects showed deviations in the cardiac function tests—hypotonia, hypertonia, and other regulatory disturbances. In about one-fourth, the ECG showed deviations from normal.

In the majority of the cases, control studies showed retrogression of these disturbances in the course of one to two years. Whether the disappearance of obvious

pathologic signs indicates complete recovery, or whether an eventual higher mortality is to be expected remains to be seen.—C.-J. HOWELL

Parotitis as a sign of protein deficiency and disturbed protein metabolism is suggested in the following paper.

A New Sign of Malnutrition. Deficiency Parotitis due to Elective Nitrogen Deficiency. H. Gounelle. *Bull. et mém. Soc. méd. d. hôp. de Paris* 22 & 23: 866, 1952.

The author considers as a new specific sign of malnutrition the parotitis persisting in undernourished subjects during convalescence from exhausting illnesses such as bacillary dysentery or in precachectic or cachectic states. He particularly incriminates deficient dietary nitrogen and the protein disturbances it produces in the organism. The repercussions on water metabolism may explain these inflammatory episodes in the salivary glands. The data militating in favor of this parotitis from nitrogen deficiency are reviewed.—H. TEULON

The following very interesting case is another illustration of abnormal protein synthesis, the clinical significance of which is becoming more important.

Idiopathic Hypoproteinaemic Oedema and Amino-Aciduria in an Infant. J. P. Bound and W. R. Hackett. *Arch. Dis. Child.* 28: 104, 1953.

The authors point out that hypoproteinemia may occur as a result of inadequate intake, faulty absorption, abnormal renal losses as in albuminuria, and as a result of faulty synthesis by the liver. However, in certain cases the etiology remains obscure.

The significance of the loss of amino acid by way of the urinary tract in disorders of amino acid metabolism has been adequately demonstrated in such conditions as phenylpyremic oligophrenia, cystinuria and cystinosis, galactosemia, and hepatic diseases. Apparently when edema is attributable to hypoproteinemia and aminoaciduria, galactosemia or liver disease might be expected.

This is a report of hypoproteinemic edema in a 1-month-old infant in whom this was not the case. This patient was the fourth child in the family. The first sibling also developed edema of the feet and legs at 7 weeks of age which was followed by ascites, and died at 6 months of age with hypoproteinemia.

With the use of chromatograms and electrophoretic studies, as well as standard laboratory procedures, these authors were able to demonstrate hypoproteinemia with a decrease in the A:G ratio, and an absence of gamma globulin in the plasma. However, tests of liver function were normal. There occurred an intermittent aminoaciduria with as many as 15 amino acids being demonstrated in the urine of the patient during one period of increasing edema associated with an infection. The predominant amino acids in the urine at all times were glycine, alanine, threonine, and traces of cystine.

During severe and recurrent infections, the amino acid content increased in the blood as well as in the urine.

Administration of alpha-tocopherol during a 6-week period of intermittent improvement could not be correlated with any beneficial effects. The control of infections was attributed to antibiotic and chemotherapeutic agents and the diuresis to plasma transfusions.

At approximately 1 year of age the edema was minimal, the amino acid excretion in the urine was normal or slightly elevated, and liver function tests continued to give normal results. The serum bilirubin was less than 0.2 mg. per cent, alkaline phosphatase 17 K.A. units, plasma protein 5.7 Gm. per 100 cc. with albumin 2.3 Gm. per 100 cc. Plasma gamma globulin continued to be absent, although the Shick test was negative.

Although increased aminoaciduria and elevated serum levels of amino acids suggest hepatic dysfunction as in hepatic cystinuria, no evidence of hepatic disease was discovered and galactosemia was absent.

[The value of paper chromatography and electrophoresis is evident. The absence of gamma globulin and the association of this state with recurrent infections parallels the observations of Bruton and later by Janeway as well as others in this country on agammaglobulinemia.]—J. N. ETTELDORF

Evidence has accumulated to show that uric acid is produced from glycine acetate and other simple precursors. The rate of formation of uric acid may then depend upon the availability of nitrogenous sources in the diet. This is shown to be correct by the finding of increased uric acid synthesis in the presence of a high protein intake.

A Further Study of the Utilization of Dietary Glycine Nitrogen for Uric Acid Synthesis in Gout. J. D. Benedict, T. F. Yu, E. J. Bien, A. B. Gutman, and D. Stetten, Jr. *J. Clin. Investigation* 32: 775, 1953.

N^{15}-labeled glycine was fed to 4 patients with gout and 2 normal individuals. The former differed in that 2 patients excreted large amounts of uric acid in the urine, while the remaining 2 excreted normal amounts. The 2 patients who excreted large amounts of uric acid in their urine exhibited a rapid incorporation of the N^{15} into their urine uric acid, while the other 2 showed normal excretions. From these results the authors conclude that patients with gout may be crudely classified into two types: those who synthesize uric acid rapidly in the face of normal renal function, and those who have normal synthesis and excretion of uric acid. What determines these differences or whether they are stages in the same process is not yet clear.—J. F. MUELLER

The Relation of Dietary Nitrogen Consumption to the Rate of Uric Acid Synthesis in Normal and Gouty Man. E. J. Bien, T. F. Yu, J. D. Benedict, A. B. Gutman, and D. Stetten, Jr. *J. Clin. Investigation* 32: 778, 1953.

In this paper the problem of the importance of the dietary protein in the synthesis of uric acid is studied. As in the previous study, N^{15}-labeled glycine nas been fed to one subject with gout and one normal person while on a relatively low purine diet and 10 to 12 months later while on the same diet fortified with skimmed milk powder. The amount of N^{15} appearing in the urinary uric acid and total urinary nitrogen was studied. Both in the normal and gouty subject, the administration of increased protein resulted in an increase in uric acid synthesis. It would appear from this study that dietary restriction of protein might still be a helpful tool in the clinical management of gout. —J. F. MUELLER

SIDEROSIS AND DIETARY IRON

Extensive abnormal iron deposits have been described in the viscera of certain African natives found to have malnutrition and pellagra. This unusual finding has no parallel in the pathological studies conducted in similar patients elsewhere. It has been suggested that the iron found in the organs of these patients is not related to the nutritional status, but rather to the large amounts of adventitious iron, probably derived from cooking vessels.

Siderosis in the Bantu. J. Higginson, T. Gerretsen, and A. R. P. Walker. *Am. J. Pathol.* 29: 779, 1953.

Gillman and Gillman first correlated the extensive deposition of hemosiderin (abnormal iron deposits) in the viscera of the South African Bantu with malnutrition and pellagra.

The present investigation is based on 44 necropsies representing siderotic cases of varying severity. The morbid anatomy and the histologic and chemical pattern of iron distribution are described. Differences between Bantu siderosis, classical hemochromatosis, and other instances of malnutritional siderosis are emphasized.

Gillman and others maintained that malnutrition caused hepatic damage, with deposition of hemosiderin in liver cells (cytosiderosis), followed by iron excretion in bile, consequent iron reabsorption, and widespread deposition (siderosis). The present study, however, demonstrates widespread reticulo-endothelial iron deposition from the beginning. The authors did not observe a similar histologic picture in all cases of acute pellagra on admission, which might be expected if iron deposition were a feature of pellagra in South Africa. Siderosis has not been significant in the previously published American pathologic studies on pellagrins. Varying degrees of portal fibrosis are frequent among Bantu. No correlation was found between the degree of fibrosis and the amount of iron pigment in the liver. Severe siderosis was seen without fibrosis and vice versa.

Walker and Arvidsson demonstrated large amounts of adventitious iron in the diet of the Bantu—enough to permit unrequired iron to be absorbed, retained, and deposited. The present authors conclude that the possibility of iron overload in the Bantu warrants further investigation, and are doubtful whether undernutrition, malnutrition, or pellagra can be regarded as major etiological factors.—J. GRUHN

The Effect of Habitually High Iron Intake on Certain Blood Values in Pregnant Bantu Women. T. Gerritsen and A. R. P. Walker. *J. Clin. Investigation* 33: 23, 1954.

The South African Bantu has a habitually high iron intake. Hypochromic anemia is extremely rare, and an occasionally elevated serum iron level is encountered. At necropsy there is frequently an abnormal deposition of iron in the tissues of the adult.

Pregnant Bantu women, eating a diet characterized by a very high iron content though otherwise inadequate, were found to have no significant change in hemoglobin, hematocrit, or serum iron when comparing the first and second half of the prenatal period.—S. O. WAIFE

Experimental dietary siderosis in the rat has been produced by the administration of iron salts.

Experimental Induction of Iron Overload in the Rat. Morphological Alterations Due to Dietary Siderosis. J. P. Wyatt and J. Howell. *Arch Pathol.* 55: 466, 1953.

This investigation represents a confirmation and extension of Hegsted and Kinney's work on iron accumulation which developed in rats maintained on a corngrit-iron salt diet. After 5 days the diets containing iron were supplemented with copper in half the rats.

The induced morphologic changes are described, with emphasis on the distribution of iron. Excessive iron storage was produced in rats on low protein (corngrits)-iron salt diets. After 150 days, no pigmentary cirrhosis developed. Despite the addition of copper, no difference in iron storage or fibrosis was noted. Castrated and noncastrated animals did not differ. From these experiments it would appear that some additional factor other than copper or androgen withdrawal is required to produce progressive pigmentary cirrhosis.

These observations suggest that there are a number of differences between cytosiderosis in the South African Bantu, classical hemochromatosis, and dietary siderosis (ferrichromatosis of Kinney). The relationship of these experimental findings is integrated with the whole problem of hemochromatosis.—J. GRUHN

An iron-protein precipitate formed by adding ferric chloride to milk whey was found to be as effective as

ferrous sulphate in the formation of hemoglobin in the rat. At the same time, the protein efficiency of the precipitate was equivalent to that of lactalbumin and casein.

Studies on Bovine Whey Proteins. I. Preparation of the Ferric Derivatives of Whey Proteins. R. J. Block, D. Bolling. K. W. Weiss, and G. Zweig. *Arch. Biochem.* 47: 88, 1953.

When aqueous $FeCl_3$ is added to milk whey, a precipitate forms at pH 3–4. This iron-protein precipitate is soluble in dilute alkali and is called "ferrilactin" by the authors of this paper. Purified ferrilactin is very soluble in water at pH 2 and at pH 6.5–7.5, and is not heat-coagulable at the latter pH range even after several hours' constant boiling. It contains approximately 15 per cent of iron and is readily digested by pepsin and by trypsin. The protein efficiency of ferrilactin was 3.36 under experimental conditions where lactalbumin was 3.30 and casein was 3.11. Estimation of the biological availability of the iron in ferrilactin indicated that it was approximately as valuable as $FeSO_4$ in the formation of hemoglobin by the rat. Large quantities of ferrilactin (up to 45 per cent of ration) fed to rats weighing approximately 170 Gm. over a 3-week period showed no signs of toxicity as would be indicated by a retardation of growth.—M. K. Horwitt

The problem of the dietary iron requirements of children is thoroughly discussed in the following paper. It is important to determine that the iron intake is sufficient not only to produce adequate hemoglobin, but also for the creation of adequate iron reserves.

Iron Requirements of Children. F. A. Johnston. *J. Am. Dietet. A.* 29: 758, 1953.

This interesting, well-written review outlines assumptions which are basic to current recommendations concerning iron requirements of children. It also cites existing experimental evidence, together with researches which are needed to place our understanding of this topic on a firmer basis.

Children need iron for four purposes: maintenance, growth, the replacement of blood loss, and storage. The maintenance requirement must cover continuous day-to-day losses in urine, metabolic iron in feces, skin cells sloughed off from the surface of the body, hair, nails, perspiration, saliva, tears, and nasal discharges. It is estimated that 0.3–0.4 mg. iron daily is needed for maintenance needs. Though there is no experimental method for investigating the iron requirement for growth, Heath and Patek, by estimations of the needs for increases in weight and blood volume, have suggested 0.2 mg. per day for a boy of 5 years of age and 0.4 mg. for a boy of 10 years. Children, and all others for that matter, need iron to replace blood loss—1 ml. blood contains 0.4 mg. iron.

Iron stores in adults insure against periods when diets may be deficient in iron, conditions when iron absorption may be reduced, hemorrhage, or in women for pregnancy and lactation. The needs are unpredictable. About the only way to estimate them is to determine the amount required to build stores as large as are regularly found in normal adults. Using the estimate supplied by Heath and Patek of 1300 mg. as the store in adult man and 100 mg. in the 2-year-old, 1200 mg. must be supplied during growth years. This need not be done always at the same rate. If children were to store one-eighth of the total amount between ages of 2 and 6, they would need to store 0.1 mg. a day. If girls were to store three-fourths between the ages of 6 and 12, they would store 0.4 mg./day.

The total amount children need to absorb on the basis of the above reasoning is 0.6 mg. daily for boys and 0.7 for girls at 5 years of age; 1.0 mg. for boys and 1.3 for girls at the age of 10. To this should be added an unknown allowance for a blood loss which is unpredictable.

Data indicate that children absorb only 8–28 per cent of dietary iron. If a figure of 10 per cent were used as an approximation, food should provide 6 mg. iron per day for boys and 7 mg. for girls of five and 7 and 9 mg. respectively, for 10-year-olds.

The needs of adolescent girls are higher because of rapid growth and menstrual losses. On the basis of previously published data with six girls, the authors concluded that 13 mg. iron daily is probably enough for this age.

The authors feel that hemoglobin determinations are satisfactory to tell whether the diet is adequate for current needs of children but do not tell whether enough iron is being stored to build a safe reserve for adulthood. Attention should be given to iron content of diets for infants, preschool children, elementary school children, adolescent girls, and women in the child-bearing years.—J. M. Smith

COPPER METABOLISM

Increasing evidence is accumulating to indicate the important role that copper plays in iron metabolism and in the action of certain enzymes such as tyrosinase. The metabolism of copper has been traced through its absorption and transport in the blood as a protein-bound element, ceruloplasmin. Copper is believed to act as a catalyst at some stage of hemoglobin synthesis, although proof of this role in man has not been definitely established.

Studies on the Function and Metabolism of Copper. M. M. Wintrobe, G. L. Cartwright, and C. J. Gabler. *J. Nutrition* 50: 395, 1953.

The adult human body contains 100 to 150 mg. of copper, of which about 64 mg. are found in the muscles, 23 mg. in the bones, and 18 mg. in the liver. The concentration of copper is higher in the liver than in any other organ. In the fetal liver it is 5 to 10 times that of adult liver.

Wintrobe, Cartwright, and Gabler found copper in the blood plasma and in the cells. Red cell copper tends to be constant. The plasma copper, however, increases under a great variety of circumstances. Hypocupremia is rare. By far the greatest proportion of copper is in the form of a copper protein corresponding to an alpha-globulin. A very small part of plasma copper is bound more loosely to one of several possible protein fractions and may represent copper in transit. Deficiency of copper is associated with the development of severe, hypochromic microcytic anemia, hypoferremia as well as hypocupremia, moderate leukopenia, and bone marrow normoblastic hyperplasia. In copper deficiency the movement of iron from the tissues to the plasma is decreased. Copper favors iron absorption from the gastrointestinal tract. Studies with intravenously administered radioactive iron reveal that the uptake of iron for hemoglobin synthesis is poor in copper-deficient swine.—B. SURE

In the following series of papers, the effect of copper deficiency upon the blood is described, together with a disorder of bone with the characteristics of osteoporosis.

A Bone Disorder Associated with Copper Deficiency. I. Gross Morphological, Roentgenological, and Chemical Observations. J. H. Baxter and J. J. VanWyk. *Bull. Johns Hopkins Hosp.* 93: 1, 1953.

Young dogs subsisting for several months on a highly purified diet deficient in copper developed a bone disorder characterized by abnormally thin cortices, deficient trabeculae, and wide epiphyses. Fractures and deformities occurred in many of the animals. Accompanying the bone changes there was anemia and graying of the hair. This disorder was relieved by the administration of copper and did not occur in control animals.

The blood calcium, inorganic phosphorus, and vitamin D levels of these copper-deficient animals were normal. It has been shown that this bone disorder is not a result of inactivity, inanition, or anemia, and it was specifically prevented or relieved by copper.

In this article, photographs of the dogs, roentgenograms, and gross specimens of the legs show the distinctive changes in this newly defined deficiency. —S. O. WAIFE

A Bone Disorder Associated with Copper Deficiency. II. Histological and Chemical Studies on the Bones. J. H. Baxter, J. J. VanWyk, and R. H. Follis, Jr. *Bull. Johns Hopkins Hosp.* 93: 25, 1953.

Microscopic studies of the tissues of the aforementioned copper-deficient dogs indicate that in this syndrome there was excessive absorption of bone, particularly about the inner portions of the cortex and also in the shaftward portions of the metaphyses. Decreased deposition of bone matrix also may have occurred. These changes did not appear to be related to bone marrow hyperplasia. Chemical studies on cortical bone show that ash, calcium, phosphorus, and carbon dioxide were normal in both control and copper-deficient dogs. The residual calcium, Ca: P ratio and the ratio of calcium phosphate to calcium carbonate were almost identical in the two groups. These authors conclude that the bone disorder is a diffuse osteoporosis with no primary disturbance in calcification.—S. O. WAIFE

The Anemia of Copper Deficiency in Dogs Compared with That Produced by Iron Deficiency. J. J. VanWyk, J. H. Baxter, J. H. Akeroyd, and A. G. Motulsky. *Bull. Johns Hopkins Hosp.* 93: 41, 1953.

As a result of iron deficiency in dogs, the peripheral blood shows relatively normal numbers of red blood cells but with a marked decrease in red cell size, hemoglobin content, and hemoglobin concentration. In the marrow, iron deficiency results in a hyperplasia of hemoglobin-deficient normoblasts. There is no appreciable shift to the left, or evidence of maturation arrest. This is the expected result and is explained on the basis of a hemoglobin deficiency.

On the other hand, in experimental copper deficiency there was a reduction in the number of erythrocytes but with the maintenance of relatively normal indices. Furthermore, in the marrow there was no evidence of hemoglobin deficiency but there was evidence of defective development of the red cells. The results would indicate that, at least in the dog, copper is essential for the normal maturation of the erythrocytic elements of the marrow and the production of normal numbers of red cells.—S. O. WAIFE

SCURVY AND ASCORBIC ACID METABOLISM

The clinical syndrome resulting from ascorbic acid deficiency is encountered in adult patients whose intake of this vitamin has been restricted over long periods because of poverty, food faddism, alcoholism, and chronic disease states. In adults, as well as in infants, anemia is one of the findings associated with this condition. Previous abstracts in this JOURNAL *(1: 260) have dealt with the relationship between folic acid, vitamin B_{12}, and ascorbic acid with respect to hematopoiesis. Adult patients found to have scorbutic anemia have shown an adequate response to ascorbic acid.*

The Anaemia of Adult Scurvy. B. Bronte-Stewart. *Quart. J. Med.* 22: 309, 1953.

Over a four-year period, in Capetown, 32 adults were admitted with the diagnosis of scurvy. Co-existing deficiencies, or other diseases, were surprisingly rare. From this detailed survey of the patients it appears that anemia was present in high incidence in adult scurvy, and this anemia can be quite severe.

The anemia was normochromic and normocytic, but occasionally macrocytic in the more severe cases. As the anemia progressed there was more variation in the size and hemoglobin content of the erythrocytes. Reticulocytes may or may not be present in the more severe cases. The bone marrow often showed decreased mitosis although hypercellular in appearance. Occasionally, megaloblasts were seen. An increased excretion of pigment was due to extravascular hemolysis in hematomata but superficially resembled a hemolytic anemia. There was a low plasma iron and iron-binding capacity which appeared to be caused by the hematomata.

A prompt and complete hematologic response followed the addition of ascorbic acid alone to the same diet on which the disease developed. This response was seen without the need for an increased intake in other vitamins, iron, or extrinsic factor. Folic acid, vitamin B_{12}, and intravenous iron failed to have any influence on the bone marrow or peripheral blood picture. Of the 26 anemic patients in the series, none failed to respond to synthetic ascorbic acid.

The authors note that, considering the small daily requirements and the fact that bed rest will "release more vitamin C for erythropoiesis," some hemotalogic remission may be expected when the patient is kept at rest. This points out the necessity for a preliminary period of bed rest before other measures are tried. The anemia of scurvy may be produced by the increased demand for vitamin C by infections or other diseases. On morphologic grounds, furthermore, it is difficult to differentiate the anemia of adult scurvy from other deficiency anemias. The appearance of the peripheral blood smear, the leukopenia, the histamine-fast achlorhydria, and the occasionally associated megaloblastic bone marrow may suggest the erroneous diagnosis of pernicious anemia.—S. O. WAIFE

The radiographic manifestations of scurvy in infancy have been well recognized. In the following paper calcification of the hematomata seen in the subperiosteum appears to undergo changes resulting in restitution to normal bone following treatment.

Some Radiographic Manifestations of Early Scurvy. J. F. Brailsford. *Arch. Dis. Child.* 28: 81, 1953.

Early radiographic signs of scurvy, namely, fracture and hematoma, may be seen before clinical manifestations are reported. According to the author, amorphous calcification of the hematoma may occur before treatment is instituted. He states that, "within the first few months of life radiographs may show amorphous calcium deposition in haematomata enveloping one or more long bones which appear to have normal structure and density, and, though no other definite indication of scurvy may be present, organization, ossification, and complete restitution to normal bone takes place readily on the administration of vitamin C."

Case reports of unusual hematomata associated with osteogenesis imperfecta, and in association with paralyzed limbs are included and have been attributed by the author to vitamin C deficiency.

Although the author has seen few cases of cortical hyperostosis (Caffey—Smythe Disease), he apparently feels that hematoma formation and calcification due to vitamin C deficiency is an important etiological factor.

[Although radiographs of the long bones of an infant age 3 months with early scurvy are shown, it is generally accepted that scurvy is a deficiency disease occurring at the 5th and 6th month of life. Evidence that deficiency factors act upon the fetus during intrauterine life must be extremely meager and questionable. Furthermore breast-fed babies have not been observed to develop vitamin C deficiency.

It has been my experience to observe one patient in whom the cortical thickening occurred, disappeared, and then recurred while vitamin C intake was adequate. The mandible which is usually involved in hyperostosis with or without other bony involvement has never in my experience been the site of involvement in scurvy.]—J. N. ETTELDORF

Ascorbic acid deficiency as one cause of asthenia is discussed in the following paper. Improvement of this condition was noted following the administration of 0.5 Gm. vitamin C daily.

Asthenic States and the Systematic Measurement of Plasma Ascorbic Acid. L. Guibert and R. Preaut. *Presse méd.* 60: 135, 1952.

The authors give an account of results obtained with vitamin C treatment of a group of 64 young persons suffering from disturbances associated with physiologic or mental deficiencies. The measurement of plasma ascorbic acid revealed an abnormally low level in the majority of these subjects.

The administration of 0.5 Gm. of vitamin C daily brought about a remarkable rise in the plasma vitamin level and a clear improvement in physical and psychological tests.

After discussing the value of the measurement of plasma ascorbic acid, the authors recommend the systematic practice of this determination in asthenic states, with or without associated syndromes. This will permit the demonstration of a deficiency state (which often goes unnoticed) and the institution of vitamin therapy.—H. GOUNELLE

Excessive menstrual bleeding has been attributed to a deficiency of ascorbic acid. Following the administration of the vitamin menorrhagia was corrected. The difficulties in controlling such an investigation would be multitudinous, so that further confirmation is required.

Hypermenorrhea Due to Scurvy. G. E. Morris. *Postgrad. Med.* 14: 443, 1953.

Four women were seen for uterine bleeding, in whom a deficiency of ascorbic acid was believed to be the cause. An 18-year-old girl with hemorrhagic scratch marks, positive tourniquet test, and a low vitamin C level in the blood received 300 mg. of ascorbic acid daily plus fruit juice. There was rapid improvement in the menorrhagia. Essentially similar reports were obtained from three other cases. Morris believes that scurvy is still a common condition and that all cases of prolonged or abnormal menstrual bleeding of unknown origin should be considered in this respect. It is suggested that vitamin C can affect menstrual bleeding even when the blood level appears to be within normal limits. This work needs confirmation.—S. O. Waife

Ascorbic acid was found to inhibit peptic proteolysis in vitro. *However, there is no evidence that such an effect would be obtained* in vivo.

A Study of the Effect of L-Ascorbic Acid on Gastric Digestion in Vitro. A. W. Breidenback and F. E. Ray. *Gastroenterology* 24: 79, 1953.

The effect of ascorbic acid on aerobic and anaerobic digestion of casein at pH 2 was studied *in vitro*. Amino nitrogen and ascorbic acid analyses indicated that ascorbic acid retarded peptic proteolysis when crude pepsin was employed but no inhibitory effect was observed when crystalline pepsin was used. The authors suggest that crude pepsin contains an inhibitor which is activated by ascorbic acid. The reviewer agrees with the authors that these observations must be confirmed by performing similar experiments *in vivo* but would suggest that statistical analysis of such data is mandatory. It might also be pointed out that crystalline pepsin differs chemically and electrophoretically from the protein in freshly secreted canine and human gastric juice—S. H. Lorber

The sparing effect of ascorbic acid upon the adrenocortical hormones may involve the retarding of metabolism and inactivation of these steroids by the vitamin. Evidence favoring this concept has now been accumulated with respect to the metabolic actions of the cortical hormones upon carbohydrate metabolism.

Influence of Ascorbic Acid on the Metabolic Actions of Cortical Hormones: Carbohydrate Metabolism. H. Bacchus and M. H. Heiffer. *Am. J. Physiol.* 172: 276, 1953.

This study deals with the influence of ascorbic acid on the insulin tolerance of rats treated with cortical hormones. Ascorbic acid increases the insulin tolerance of adrenalectomized rats treated with cortisone. Findings were similar in adrenal demedullated rats treated with corticotrophin. Ascorbic acid by itself does not affect insulin tolerance. Studies of urinary glucose and nitrogen show that both are increased after cortisone. When ascorbic acid is combined with cortisone the excretion is still further augmented. The authors suggest that the data indicate that ascorbic acid increases the ability of cortisone to deposit glycogen in the liver. The vitamin increases the gluconeogenic ability of cortisone.—M. J. Oppenheimer

PYRIDOXINE

The essential nature of pyridoxine in human metabolism has been established recently. Vilter estimates the human requirement for this vitamin for the adult at close to 2–3 mg. per day; other investigators (including György) feel it is too early for a definite pronouncement. Fortification of a milk substitute used for infant feeding has been found necessary because of the destruction of pyridoxine in the process of manufacture. Recently changes have been observed in the arterial walls of experimental animals deprived of dietary pyridoxine. On the other hand, a high pyridoxine intake failed to inhibit atherosclerosis in chickens.

Effect of High Pyridoxine Intake in Cholesterol-Fed Chicks. W. McFarland. *Arch. Pathol.* 55: 503, 1953.

Rinehard and Greenberg had observed the development of atherosclerosis in monkeys on low pyridoxine diets. It has been well documented that a high cholesterol and normal pyridoxine intake will result in atherosclerosis in certain experimental animals. In the present experiment on 24 white leghorn cockerels, aged five weeks, McFarland demonstrated that high pyridoxine intake failed to inhibit atherosclerosis in chickens fed cholesterol and seemed to enhance the lesions.—J. Gruhn

Pyridoxine deficiency in rats produced certain biochemical changes, among them a fall in the levels of plasma glutamine and a rise in blood urea.

Studies on Vitamin B_6. I. Biochemical Changes in Vitamin B_6 Deficiency in Rats. J. R. Beaton, J. L. Beare, J. M. White, and E. W. McHenry. *J. Biol. Chem.* 200: 715, 1953.

The blood levels of amino nitrogen, sugar, hemoglobin, and urea, plasma levels of glutamic acid and glutamine, serum protein levels, and nitrogen excretion were determined on rats which were fed 100 μg. of desoxypyridoxine per day, and the results compared with data obtained from animals which received 50 μg. of pyridoxine hydrochloride per day. No evidence of anemia as a consequence of vitamin B_6 deficiency was observed, nor was there any significant effect on the fasting blood levels of sugar or amino nitrogen. There was a marked fall in the fasting levels of plasma glutamine and a significant increase in the fasting levels of blood urea. Neither of these results could be explained by inanition, since pair feeding was employed. The pyridoxine-deficient

rats exhibited a less positive nitrogen balance than the pair-fed controls. The elevation of blood urea levels characteristic of the rats which received desoxypyridoxine was investigated in order to determine whether this elevation was a consequence of renal failure. A modified urea clearance test gave no evidence of renal damage.—M. K. HORWITT

Effects of Adrenalectomy and of Adrenal Cortical Extract in Pyridoxine-Deprived and Supplemented Rats. J. L. Beare, J. R. Beaton, F. I. Smith, J. M. White, and E. W. McHenry. *Am. J. Physiol.* 175: 21, 1953.

As a result of these experiments the authors suggest that the hormones of the adrenal cortex have no effect on the utilization of pyridoxine. The vitamin is not needed for the action of these substances in rats. Acrodynia was prevented by adrenalectomy. On the other hand, the metabolic disturbances resulting from pyridoxine deprivation were not prevented by adrenalectomy.—M. J. OPPENHEIMER

Oxidative Metabolism of Normotensive and Hypertensive Rat Tissues. N. S. Olsen. *Am. J. Physiol.* 175: 129, 1953.

Broken cell preparations from a constricted kidney of a hypertensive rat had a much smaller oxygen uptake than its fellow of the opposite side. The uptake of the constricted kidney was increased by vitamin B_6. Oxidation of amino-acids and amines was depressed by preparation of the constricted kidney. Pyridoxal did not change these results.—M. J. OPPENHEIMER

Pyridoxine has been found to be required for the conversion of tryptophane to nicotinic acid, in relation to its activity as a transaminase factor. One of the intermediary products in these reactions is xanthurenic acid. In pyridoxine deficiency abnormal amounts of xanthurenic acid are excreted in the urine, so that pyridoxine deficiency can be assayed by means of a loading dose of tryptophane. The results of such a study conducted in pregnancy follow.

Disturbance of Vitamin B_6 Metabolism in Pregnancy. M. Wachstein and M. T. Gudaitis. *J. Lab. & Clin. Med.* 42: 98, 1953.

Ninety-six per cent of 106 pregnant women at term (100 of this group were normal) excreted abnormally high quantities of xanthurenic acid in the urine following an oral load of ten grams of *dl*-tryptophane. This finding paralleled that of subjects known to be deficient in vitamin B_6 and, in 4 pregnant women, was uninfluenced by prior administration of a mixture of thiamine, riboflavin, and nicotinic acid. Short- or long-term administration of pyridoxine hydrochloride, however, prior to tryptophane loading appeared to significantly reduce xanthurenic acid excretion. Thus it was strikingly depressed in 7 subjects by providing 10 mg. of pyridoxine hydrochloride daily for several days or weeks prior to term. The interpretation is preferred that daily administration of 10 mg. of pyridoxine hydrochloride during pregnancy is advisable.

In the abstracter's opinion, this therapeutic inference presupposes the unproved theory that lowering xanthurenic acid excretion affords some advantage. In point of fact, the assumption that a "high" (for the nonpregnant state!) urinary excretion of xanthurenic acid may be desirable and a lowered excretion deleterious has not been excluded. Who would argue that the usually "high" concentration of protein-bound iodine in the serum of pregnant women, in contrast to the nonpregnant female, should be reduced by the administration of goitrogenic drugs?—R. TARAIL

ITEMS OF GENERAL INTEREST

Individual Variations in the Metabolic Cost of Standardized Exercises: The Effect of Food, Age, Sex and Race. K. Mahadeva, R. Passmore, and B. Woolf. *J. Physiol.* 121: 225, 1953.

Fundamental for any problem in human metabolism is caloric requirement. This, in turn, is directly related to physical activity. Recent attempts at establishing a normal basal metabolic rate have fixed standards in relation to sex, stature, age, climate, and race. There are little or no data on the effect of these factors on metabolism during muscular activity. If metabolic variations of the same order occurred during exercise, they would profoundly affect the food requirements of a population.

The energy expenditure of 50 persons of different sizes and ages, both European and Asiatic, was studied. One determination was made while a stepping test was performed in which measurable external work was done in raising the body weight, and the second, in walking on a level.

Statistical analysis of the data shows that the energy expenditure during stepping or walking can be very closely predicted from a knowledge of body weight, and that no significant increase in precision is gained by also taking into account height, age, sex, race, or resting metabolism. In the case of stepping, energy expenditure appears to be directly proportional to body weight. In walking, the regression line is also linear but does not pass through the origin in the charts.

In a large number of industrial, domestic, and other activities, the major part of the metabolic cost is expended in moving the body. Since weight appears to be the only important individual variable in determining the metabolic cost, the assessment for caloric needs is made more simple.—S. O. WAIFE

The Accuracy of Basal Metabolism Determination in the Clinical Laboratory. M. J. Karvonen and M. Niemi. *Scand. J. Clin. Lab. Investig.* 4: 112, 1952.

In a statistical analysis of 100 duplicate determinations of the basal metabolic rate, it was found that the methodological error was 4.4 per cent. The BMR values obtained during the summer months were significantly lower than during the remaining part of the year.—S. O. WAIFE

Blood Glucose Changes in the Newborn—Part I. R. D. G. Creery and T. J. Parkinson. *Arch. Dis. Child.* 28: 134, 1953.

Blood glucose levels were determined in normal full-term infants after an uneventful birth from healthy unanesthetized mothers. Analgesia during labor and delivery consisted of one or more of the following agents: (1) self-administered nitrous oxide; (2) 100 mg. pethidine HCl orally or intramuscularly; (3) a mixture of chloral hydrate and potassium bromide and nepenthe. Blood glucose levels were determined by the method of King and Garner requiring 0.05 ml. The accuracy of the method at low glucose levels has been substantiated.

The mother's blood (capillary) was analyzed at the time of crowning and samples were then taken from the umbilical vein and, less frequently, from the umbilical artery. Subsequent blood samples were obtained at 30-minute intervals during the first 3 hours of life, and at 3-hour intervals thereafter. Food and fluids were withheld. It was observed that the blood sugar concentration at the time of birth was similar to that of the mother but fell precipitously during the first hour of life from a mean of 79 mg. per cent to 52 mg. per cent and was maintained at "varying constancy" by individual babies. No distinct pattern was apparent after the maternal circulation was discontinued. The normal blood glucose after one hour of age ranged between 30 and 75 mg. per cent.

There is no difference between blood glucose levels of males and females.

[Again it has been demonstrated that there occurs a wide variation in the blood glucose levels in the newborn. Although efforts were made to control as many factors as possible, there still are uncontrollable variables such as endocrine secretions, muscular activity, glycogen reserve, liver function, etc., which make it difficult if not impossible to predict the level of blood sugar in these infants. The values reported by these authors are in agreement with those generally recognized for the newborn infant. At 30 mg. per cent one might anticipate some signs and symptoms of hypoglycemia, although the newborn characteristically tolerates lower blood sugar levels without symptoms than do individuals beyond this period of life.]—J. N. ETTELDORF

Comparative Studies of the Effect of Honey and Invert Sugar on Blood Sugar. H. Stadler. *D. Ztschr. f. Verdauungs- u. Stoffwechselkrankheiten* 12: 108, 1952.

The effect on the blood sugar of equal amounts (25 Gm.) of orally administered invert sugar and honey was determined in a series of normal subjects and patients with various diseases. Blood sugar determinations were made by the Hagedorn-Jensen method.

In metabolically normal subjects, the behavior of the blood sugar was not uniform. Sometimes the rise was higher after honey than after invert sugar; sometimes it was lower.

In patients with liver disease, honey often produced a higher blood sugar level than did invert sugar. In diabetics, there was little difference in the effect of the two substances. Occasionally, a high blood sugar rise occurred after honey, which was not the case after invert sugar. This rise was not accompanied by the excretion of any substantial amount of sugar in the urine. Urinary sugar excretion was greater after invert sugar. This discrepancy may perhaps be accounted for by the smaller portion of fructose in honey, or by the cholinergic factor it contains. Although the cholinergic component in honey has a weaker effect than choline itself, following parasympathetic stimulation it impedes the action of sugar.

According to this author, there seem to be no therapeutic indications for the administration of honey in diabetes mellitus.—C.-J. HOWELL

Evidence of an Inherited Factor in Trophopathic Hepatitis. A. J. Lea. *Brit. J. Nutrition* 7: 224, 1953.

It is well known that dietary insufficiency in experimental animals can produce necrosis of the liver parenchyma, with subsequent development of fibrous tissue. It was, therefore, not surprising to find evidence of permanent liver damage in service personnel who had been prisoners of war in Japanese hands. The condition apparently appeared at random, and while a few men in each camp developed it, the majority—presumably on the same diet—did not do so. In an attempt to find an explanation of this curious distribution, all possible facts relating to these cases were recorded, and it was found that the only factor that appeared to have any relationship to the incidence of liver damage was the degree of pigmentation of the eyes and hair of the individual. Those with dark hair and eyes were statistically more prone to liver damage. This implies an inherited liver abnormality linked in some way with pigmentation. This abnormality appears to be physiological rather than anatomical. It is suggested by the authors that such an abnormality would account for the irregular incidence of liver damage in cases of frank malnutrition and cases of cirrhosis, in which there is no evidence of external factors, occurring among the inhabitants of the western hemisphere. No such evidence has been found in cases of hepatitis due to chemical poisons, etc. These findings are not conclusive and are to be considered as a basis for further investigation.—B. SURE

Hepatic Tumors Due to Prolonged Ethionine Feeding. H. Popper, J. de la Huerga, and C. Yesinick. *Science* 118: 80, 1953.

Ethionine (α-amino γ-ethylthiobutyric acid) is an analogue of methionine and one of its biological antagonists. The feeding of this substance in the diet to female rats has been shown to produce severe liver damage with a cytological appearance characteristic of irregular regeneration. This lesion, which may be due to an interference with amino acid metabolism, has been reported to occur only in female rats.

The ability of prolonged feeding of ethionine to result in tumor formation was investigated by placing female rats upon synthetic diets with either 0.5 or 0.2 per cent ethionine. All of the diets also contained 0.4 per cent methionine. Cholangiofibrotic or cholangiomatous nodules of the bile duct developed as the result of the ethionine feeding. These were characterized by the piling up of epithelial cells and hyperchromasia of the cytoplasm and nuclei. The hepatomata observed consisted of nodules in which the cells had large vesicular nuclei and loose, eosinophilic cytoplasm. The pancreas of the ethionine-fed animals also showed pathological changes. It could not be ascertained whether the tumor formation was caused by ethionine or whether the persisting injury to the liver cells and bile ducts was responsible for an excessive regeneration.—M. K. Horwitt

Diet and Dental Health. D. F. Radusch. *J. Am. Dietet. A.* 29: 555, 1953.

This article reviews some of the current literature concerning the importance of diet to dental health. The author states that the problem of diet as related to dental status is, first, its effects on the original structure of the teeth; second, on the oral environment; and third, on the structure and maintenance of the supporting or periodontal tissues of the teeth.

Control of dental caries must start before improper dietary habits have been established and before the teeth are formed. We need fuller appreciation that the nutritional status of the mother before and during pregnancy is important. The health and diet of the infant have direct and indirect effects upon the structure of the teeth. A substantial share of the permanent upper and lower front teeth and of the first molars forms during this early period. The dentin and enamel of deciduous teeth start calcifying about the fourth fetal month. Many researchers show that nutrition is important in the quality of teeth formed. From birth to approximately 8 years of age the permanent dentition is forming. The adequacy of the child's diet during this period is highly significant. Studies of teeth of European children during and after the war indicate that those whose teeth developed during a period of low sugar intake showed caries reduction in the postwar period when sugar consumption was again high.

Diet affects oral environment as well as tooth structure. Action of refined carbohydrates has been studied in this connection and it is now generally accepted that reduction of sugar in the diets of caries-susceptible patients reduces caries. This should not lead nutritionists to advise reduction of sugar only, but rather to provide a postnatal diet adequate in all nutrients which will then reduce the proportion of sugar.

Another area of study has been the effect of diet upon the potential protective action of saliva. Saliva from different mouths shows intriguing variations, e.g., saliva from caries-susceptible mouths will dissolve more calcium than caries-immune; differences in ammonium or urea content have been demonstrated; there is a difference in buffering activity. The use of radioactive substances promises to bring results in investigations of dietary influences. Radioactive iodine was found widely distributed in a patient's tooth 5 hours after administration in a glass of water. The author mentions evidence that cleansing of teeth will reduce incidence of decay.

Diet also affects the structure and maintenance of tissues around the teeth. An inverse relationship has been reported earlier by the author between the food-calcium intake and the degree of periodontal disease. Soft tissues are affected by dietary practices, as evidenced by the oral symptoms of scurvy and the sore mouths associated with low intakes of the B vitamins. Linghorne *et al.* demonstrated that those adult men who ingested at least 75 mg. ascorbic acid a day were much less likely to have recurrence of a previously treated gingivitis than those whose intake was no more than 25 mg.

Good dental health does not only concern the teeth. Only when the supporting tissues are sound can the natural denture serve comfortably throughout life. Thus diet is significant at all ages.—J. M. Smith

New Aspects of the Treatment and Etiology of Multiple Sclerosis. P. Ervenich. *Ärzt. Forsch.* 7: 55, 1953.

During the famine years of the last World War, many instances of severe thiamine deficiency were observed in which the clinical picture was similar to that of multiple sclerosis. The response to parenteral thiamine was, in these cases, rapid and striking. It occurred to the author that, even in normal nutritional circumstances, some endogenous defect of thiamine metabolism might produce the symptom-complex of multiple sclerosis. However, the administration of thiamine to patients with multiple sclerosis did not give positive results. A few cases showed slight but unmistakable regression of the signs, but other patients were not influenced at all. When phosphorylated thiamine (cocarboxylase) became available, it was decided to test the efficacy of this form of vitamin B_1 in the treatment of this disease.

Sixty-seven patients with multiple sclerosis (39 female and 28 male), most of them severe, chronic cases, received Berolase® (phosphorylated thiamine). Of these, 50 responded to the treatment, some of them dramatically. The first signs of a response

usually appeared after 6 to 8 days of treatment, often earlier. Thiamine was given simultaneously to some of the patients. Only the phosphorylated form was effective and the improvements achieved with it could not be maintained by thiamine alone, even in doses of 200 mg. a day.

Three remarkable case histories are presented in detail. In none of these had the duration of the disease exceeded 3 years, and the author feels that the prospects are best in such patients. However, he reports retrogression of various signs in cases of much longer duration.

Objective improvements achieved with cocarboxylase are summarized as follows: release of spasm; disappearance of pyramidal tract symptoms and intention tremor; elimination of paralytic signs and sensory defects; improvement of paresthesias; increase of visual power; return of control over bladder and rectum; and improvement in overall strength and walking ability. The fact that even long-standing cases gave objective evidence of retrogression of various pathologic signs leads the author to feel that phosphorylated thiamine is superior to anything so far discovered as a therapeutic measure in multiple sclerosis, and that it may be possible to prevent the development of chronic cases by early, long-term treatment with this agent.

In 57 of the 67 patients, pretreatment pyruvic acid levels were found to be higher than normal before or after glucose. These findings, indicative of a disturbance of the oxidative metabolism of pyruvic acid, suggest a basis for the effectiveness of phosphorylated thiamine and for the failure of simple thiamine. Although the details of pyruvic acid metabolism are not yet entirely clear, it is certain that thiamine, among other regulators, is indispensable to it, and that in its phosphorylated form (cocarboxylase) it catalyzes the metabolism of pyruvic acid. In the 10 cases in which pyruvic acid levels were within normal limits, it is suggested that there was compensation by other regulators of pyruvic acid metabolism. —C.-J. Howell

[*Ed. note:* Multiple sclerosis is notorious for its "spontaneous" remissions and relapses, making evaluation of therapy by any agent extremely difficult. Obviously, other studies along these lines are urgently needed.]

Maintenance Therapy of Pernicious Anemia with Vitamin B_{12}. G. C. Meacham and R. W. Heinle. *J. Lab. & Clin. Med.* 41: 65, 1953.

Forty-three patients with pernicious anemia were treated with either 3 μg. Vitamin B_{12} concentrate, or 1 μg. of crystalline Vitamin B_{12} given by injection every 3–4 weeks for 11 to 16 months. Many of these patients had shown previous hematologic relapses of moderate degee while receiving 1 μg. daily of Vitamin B_{12} concentrate. All patients who previously had suboptimal erythrocyte and hemoglobin levels showed improvement. No added benefit was obtained from purified liver extract. Macrocytosis persisted, however, and was not eliminated by therapy with purified liver extract or folic acid. From the observations in this study it appears that vitamin B_{12} in adequate dosage is no less effective than purified liver extract in the management of patients with pernicious anemia. —R. W. Vilter

Correction of Anemia Following Hypophysectomy by Administration of Cobalt. J. F. Garcia, D. C. Van Dyke, and N. I. Berlin. *Proc. Soc. Exper. Biol. & Med.* 80: 472, 1952.

Cobalt is said to produce polycythemia by interfering with oxidative mechanisms. Hypophysectomy interferes with the usual increase in red cells and hemoglobin in response to an environment of reduced oxygen tension. To study the interrelations of these two effects, 5 hypophysectomized rats received 0.07 mg. of cobaltous sulfate intraperitoneally. The control (uninjected) rats showed the anemia typical of hypophysectomy. The cobalt-injected hypophysectomized rats showed a 58 per cent increase in grams of circulating hemoglobin per 100 Gm. of body weight, which resulted in a normal total red cell volume and circulating hemoglobin. Apparently the pituitary is necessary for a normal erythropoietic response to hypoxia, but it is not necessary to obtain a normal erythropoietic response from cobalt. The mechanisms responsible in each case appear to differ.—S. O. Waife

Non-Protein Nitrogen Changes in Serum and Plasma of Rats Following Thermal Injury. H. Rosen and S. M. Levenson. *Proc. Soc. Exper. Biol. & Med.* 83: 91, 1953.

Following thermal injury in rats, almost the entire increase in filterable nitrogen in the sera consists of urea and free and combined amino nitrogen in their normal relationship. In the plasma ultrafiltrate of the injured rat, increases in tyrosine, phenylalanine, and histidine are noted, and decreases in other amino acids. The largest increase is made up of a compound which is probably taurine and an amino acid conjugate. The composition of the conjugate is similar in normal and injured rats.—L. W. Kinsell

On the Mode of Action of So-Called "Orizotoxin." Behavior of Thiamine in Liver and Muscles of Pigeons Treated with "Orizotoxin." U. Quatrini. *Acta vitaminol.* 6: 145, 1952.

Free thiamine in the liver was found to be about 25 per cent lower in pigeons who had received "orizotoxin" (an alcoholic extract of polished rice) than in control birds maintained for the same period on an otherwise similar regimen. These experiments would indicate that polished rice contains an alcohol-soluble substance capable of provoking a beriberi-like syndrome in pigeons in a very short time (2 to 8 days). As well as a decrease in liver thiamine, an increase in tissue pyruvic acid has been observed after administration of the alcoholic extract of polished rice. There would seem to be a thiamine-antagonistic substance in

polished rice which rapidly exhausts thiamine reserves or which impedes the formation or action of diphosphothiamine.—C. J. HOWELL

Antifatty Liver Action of Papain and Ficin in Insulin-treated Depancreatized Dogs. H. Feinberg, I. L. Chaikoff, and C. Entenman. *Proc. Soc. Exper. Biol. & Med.* 80: 161, 1952.

The development of fatty liver in insulin-maintained depancreatized dogs can be prevented by the daily administration of plant proteolytic enzymes obtained from papain and ficin. The authors conclude that this effect is identical with that observed when one feeds crystalline trypsin or raw pancreas to similar animals.—L. W. KINSELL

The Effect of Methionine in Experimental Wound Healing. A Morphologic Study. R. Perez-Tamayo and M. Ihnen. *Am. J. Pathol.* 29: 233, 1953.

The present authors report a morphologic study of experimental wound healing on 4 groups of rats: (1) normal controls, (2) no-protein diet, (3) no-protein diet with methionine supplement, (4) no-protein diet with valine supplement. The valine control was selected because valine is an essential amino acid, has the same N value as methionine, and contains no S. It was found that methionine alone added to a protein-deficient diet produced the same morphologic pattern of wound healing as in normal controls. The supplement of valine did not alter the poor wound healing noted on the protein-deficient diet alone.

From their morphologic studies, and from experiments on tensile strength, the authors conclude the effect of protein on wound healing is determined by its methionine content and that methionine plays an important role in the synthesis of connective tissue. Their results offer adequate histologic explanation for the decreased tensile strength of wounds of protein-deficient animals. The possible mechanism by which methionine acts and origin of ground substance are also discussed.

[To the lengthy bibliography, so useful to the interested student, the reviewer would like to add the model study of Levenson *et al.* (*Surgery* 28: 905, 1950).]—J. GRUHN

Certain Metabolic Effects of Niacin and Priscoline. R. G. Janes. *Am. J. Physiol.* 174: 46, 1953.

Niacin and Priscoline® when injected into fasted rats increased the excretion of urinary acetone bodies and nitrogen. Total liver lipid was unchanged. Liver glycogen was increased by niacin but lowered by Priscoline®. Larger urine volumes were excreted by the animals receiving Priscoline®. The author was unable to correlate increased urinary ketone excretion with liver fat or carbohydrate levels in heart or muscle.—M. J. OPPENHEIMER

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